COBALT(II) SCHIFF BASE COMPLEXES CATALYSED BIOMIMETIC OXIDATION OF ORGANIC SUBSTRATES WITH DIOXYGEN

A Thesis Submitted
in Partial Fulfilment of the Requirements
for the Degree of
DOCTOR OF PHILOSOPHY

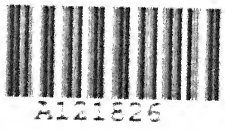
by

T. PUNNIYAMURTHY

to the

DEPARTMENT OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY KANPUR

JUNE, 1994



Dedicated

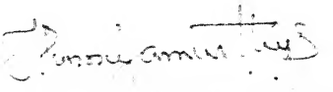
to

My Parents

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology, Kanpur, India under the supervision of Prof. Javed Iqbal.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.



T. PUNNIYAMURTHY

Kanpur

June, 1994.

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KANPUR, INDIA

CERTIFICATE-I

This is to certify that **Mr. T. Punniyamurthy** has satisfactorily completed all the courses required for the Ph.D. degree programme. These courses include :

CHM 605 Principles of Organic Chemistry

CHM 625 Principles of Physical Chemistry

CHM 645 Principles of Inorganic Chemistry

CHM 664 Modern Physical Methods in Chemistry

CHM 611 Physical Organic Chemistry

CHM 602 Advanced Organic Chemistry-II

CHM 800 General Seminar

CHM 801 Graduate Seminar

CHM 900 PG Research

Mr. T. Punniyamurthy successfully completed his Ph.D. qualifying examination in March, 1992.

(P. K. Ghosh)
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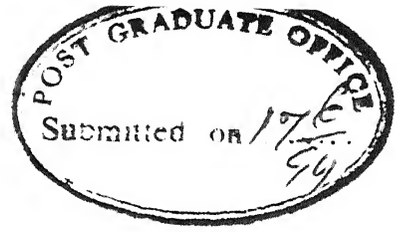


CERTIFICATE-II

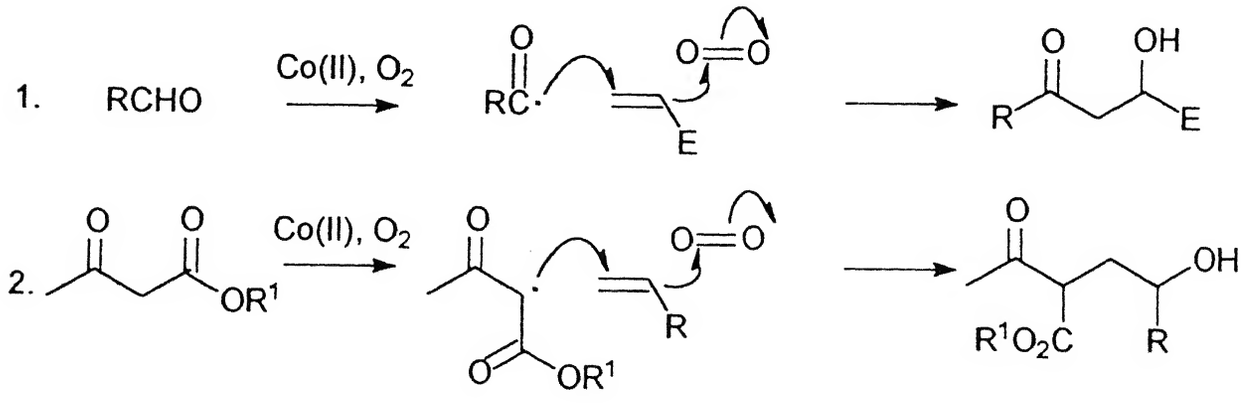
It is certified that the work contained in the thesis entitled "COBALT(II) SCHIFF BASE COMPLEXES CATALYSED BIOMIMETIC OXIDATION OF ORGANIC SUBSTRATES WITH DIOXYGEN" has been carried out by Mr. **T. Punniyamurthy** under my supervision and the same has not been submitted elsewhere for a degree.

(Javed Iqbal)
Professor
Department of Chemistry
I.I.T. Kanpur

Kanpur
May, 1994

Abstract

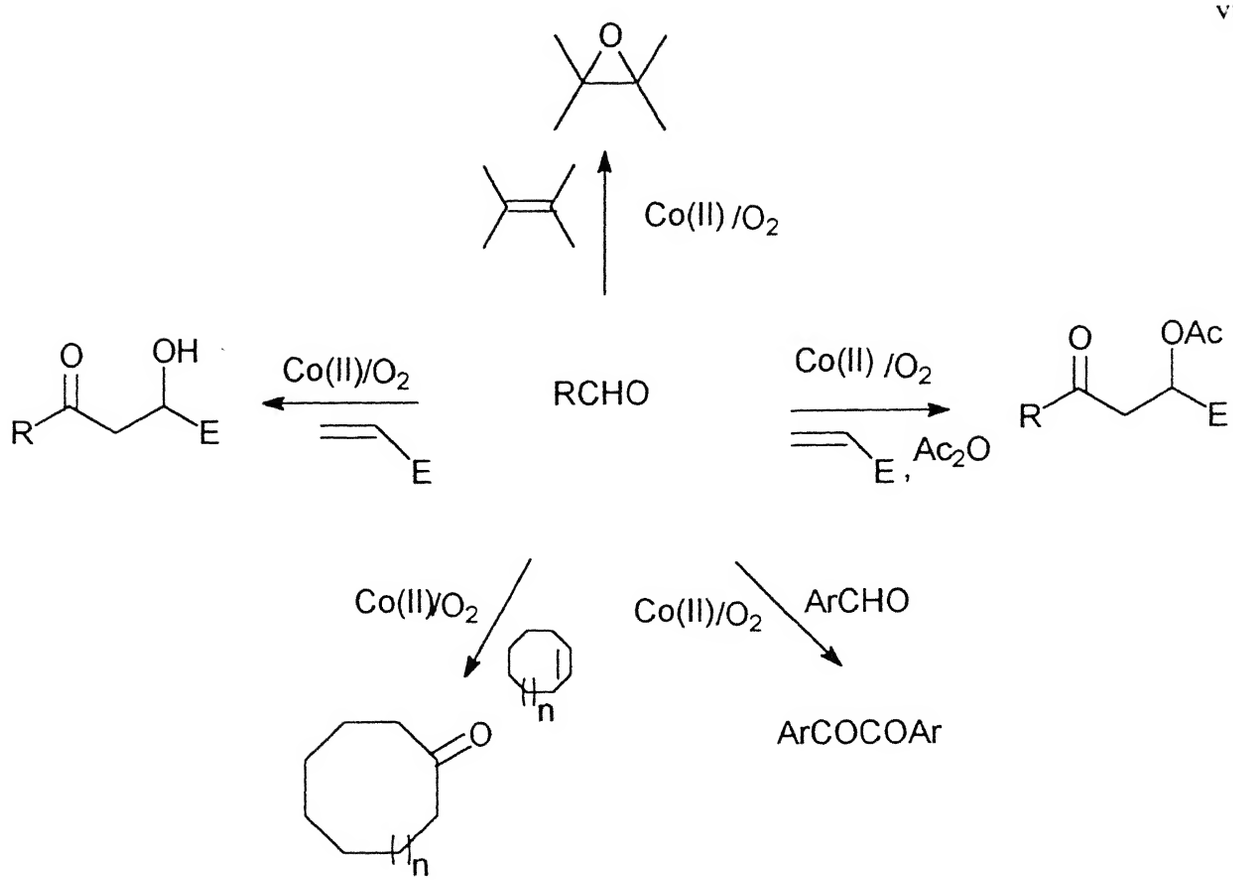
This thesis describes cobalt(II) Schiff base catalyzed oxygen transfer reactions to organic substrates in the presence of carbonyl compounds which facilitates this process. The results of the thesis is based on two major reactions and the chemistry of these can be depicted as shown below:



The thesis is broadly divided into two parts:

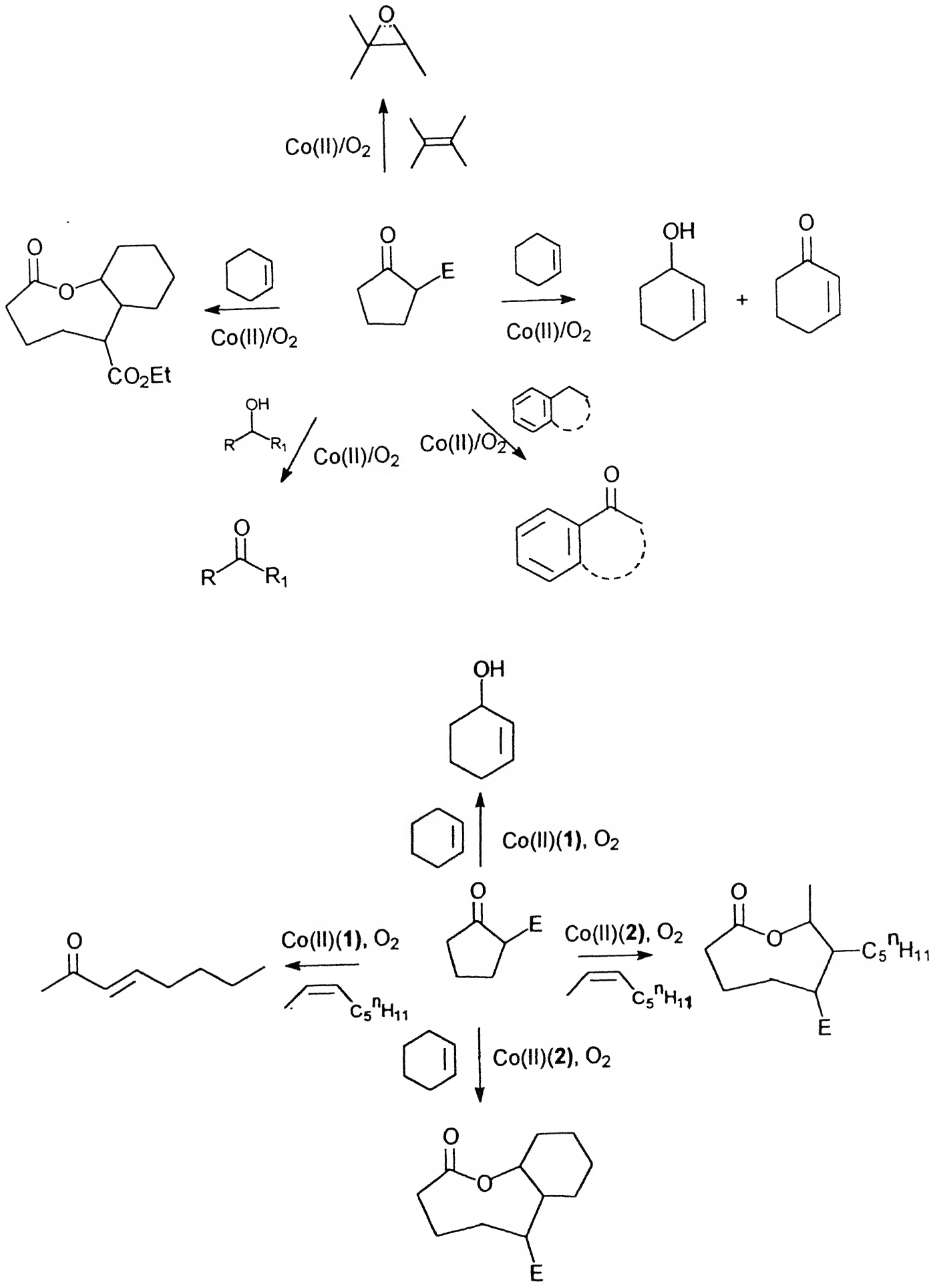
Part One: Cobalt Catalyzed Generation and Reactivity of Acyl Radicals from Aldehydes in the Presence of Dioxygen

This section deals with generation of acyl radical from aliphatic aldehydes in the presence of dioxygen and cobalt(II) Schiff base catalysts. The acyl radical generation is only possible in the presence of oxygen and the latter takes part in the reaction with organic substrates. The exploration on the reactivity of the acyl radical has been described in this section and the summarized version is given below:



Part Two: Cobalt Catalyzed Generation and Reactivity of 1,3-Dicarbonyl Radical from β-Ketoesters in the Presence of Dioxygen

This section deals with the generation of 1,3-dicarbonyl radical from the corresponding β-ketoester in the presence of dioxygen and catalytic amount of cobalt(II) Schiff base complexes. The reactivity of radical generated from cyclic ketoester with variety of alkenes are explored and the outcome of the reaction is dependent upon the nature of alkene. The product distribution is controlled by the nature of the catalysts as diverse products are obtained by changing the ligand on the catalyst derived from cobalt(II). A wide range of reactivity profile is exhibited by using cyclic ketoester, oxygen and the cobalt catalysts. These reactions are completely controlled by dioxygen as no appreciable reactivity is observed in its absence. The results of this section is summarized below:


Co(II)/O2
Co(II)/O2
Co(II)/O2
Co(II)/O2
Co(II)/O2
CO2Et
OH
R
R1
Co(II)(1), O2
Co(II)(2), O2
Co(II)(1), O2
Co(II)(2), O2
C5nH11
C5nH11

ACKNOWLEDGEMENT

I am extremely grateful to Professor Javed Iqbal for his expert guidance, encouragement and suggestions in interesting research topics throughout my research career. His unfounding enthusiasm, and zeal for research has inspired me immensely and has been a pleasure for me to have the benefit of his invaluable training in the art of organic synthesis. For these and his many other contributions, I shall ever remain profoundly indebted to him. I also take this opportunity to express my gratitude to Mrs. Iqbal, Aman and Sarah for their love and affection showed on me.

I am grateful to Professor S. Ranganathan, Dr. R.N. Mukherjee, Dr. Parimal Bhardwaj, Dr. S. Manogaran, Professor N. Sathyamurthy, Dr. A. Elias and Professor S. Sarkar for their kind help and valuable suggestions.

I gratefully acknowledge my lab colleagues Dr. Swinder, Das, Biswas, Dr. Pratibha, Dr. Beena, Madhav, Dr. Maikap, Baskar, Manoj and Dr. Vibha for their constant help.

I owe my sincere thanks to my colleagues, Dr. Sampath, Tamilarasu, Dr. Ilango, Dr. Tharmaraj, Dr. Sheela, Dr. Immi, Dr. Pandian, Dr. Bhisma, Dr. Jayaraman, Pondimani, Padmanathan, Kalyanaraman, Debalina, Tapan Lal, Dr. Manabendra, Dinu, Dr. Narendra, Venki, Kuppi,. Jeyaraj, Kumaresan, Karum and all others for their valuable help and pleasant company.

I am also thankful to my friends, Swamy, Palani, Umamahesh, Kamal, Venket, Susil, Debanath for their support and encouragement.

I am grateful to Madhav, Dr. Beena, Dr. Swinder, Dr.Tharmaraj, Dr. Sheela, Dr. Sampath, Venki and Kuppi for proof reading of the thesis.

I am thankful to Mr. Om Prakash for his ready and unreserved help in the lab. I will be failing in my duty if I do not thank Misraji for the same.

I sincerely acknowledge the help received from Mr. Nayab Ahamad and Mr. Kanaujia for recording the IR, ^1H NMR, EPR spectra and elemental analysis.

I owe my thanks to RSIC, CDRI, Lucknow for providing me C, H, N analysis, 400 MHz ^1H NMR and Mass spectra.

My special thanks go to Dr. Swinder and his family members for their love and affection showed on me.

Finally, my heartful thanks go to my parents for their sustained help and encouragement in all my academic endeavors. I feel deeply indebted to them for whatever I have achieved so far.

T. Punniyamurthy

Contents

Part Two: Cobalt Catalyzed Generation and Reactivity of 1,3-Dicarbonyl Radical from β-Ketoesters in the Presence of Dioxygen

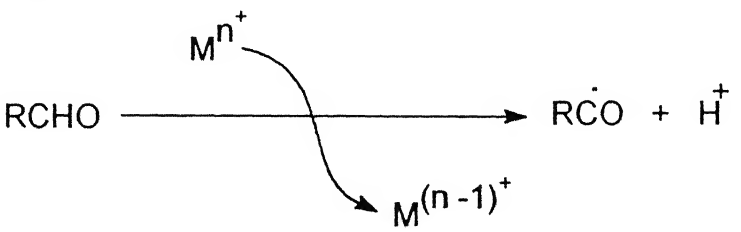
Part One

Cobalt Catalysed Generation and Reactivity of Acyl Radicals from Aldehydes in the Presence of Dioxygen

Cobalt(II) Catalysed Reaction of Enolizable Aldehydes with Alkenes in the Presence of Dioxygen: The Role of Acyl Radical

1.1 Introduction

The oxidation of aldehydes with transition metal complexes is known since long time. The aerial oxidation of aldehydes is catalyzed by traces of iron, copper, cobalt and manganese salts. Haber and Willstater[1] have proposed an initial direct interaction between metal catalyst and aldehydes (Eq. 1).



Eq. 1

A detailed investigation of metal catalyzed autoxidation of acetaldehyde[2-3] and benzaldehyde[4-5] has been carried out by Bawn and coworkers. They have proposed the following mechanism for cobalt catalyzed oxidation of benzaldehyde (Scheme 1).

$$RC^{\cdot}O + O_2 \longrightarrow RCO^{\cdot}_3$$

$$RCO^{\cdot}_3 + RCHO \longrightarrow RCO_3H + RC^{\cdot}O$$

$$Co(II) + RCO_3H \longrightarrow Co(O_2CR)_3 + HO^{\cdot}$$

$$Co(III) + RCHO \longrightarrow Co(II) + RC^{\cdot}O + H^+$$

$$Co(III) + RCO_3H \longrightarrow Co(II) + RCO^{\cdot}_3 + H^+, \text{ etc.}$$

Scheme 1

Electron transfer oxidation of acyl radicals competes with the addition of oxygen in the metal-catalyzed autoxidation of aldehydes. The electron transfer step leads to the formation of acid anhydride by reaction with carboxylic acid in the absence of water. Copper(II) is an efficient oxidant for converting an acyl radical to the corresponding acyl cation. Thus, the mixture, copper(II) and cobalt(III) acetate, is the effective catalyst for the conversion of acetaldehyde to acetic anhydride (Scheme 2)[6].

$$Co(III) + CH_3CHO \longrightarrow Co(II) + CH_3C^{\cdot}O + H^+$$

$$Co(II) + CH_3CO_3H \longrightarrow Co(OAc)_3 + HO^{\cdot}$$

$$CH_3C^{\cdot}O + Cu(II) \longrightarrow CH_3C^{+}O + Cu(I)$$

$$Cu(I) + CH_3CO_3H \longrightarrow Cu(OAc)_2 + HO^{\cdot}, \text{ etc.}$$

$$CH_3C^{+}O + CH_3CO_2H \longrightarrow (CH_3CO_2)_2O + H^+$$

Scheme 2

The acyl radical is also capable of fragmentation as indicated by the oxidation of pivalaldehyde[7] by manganese(III) acetate (Scheme 3).

$$(CH_3)_3CCHO + Mn(III) \longrightarrow (CH_3)_3CC^{\cdot}O + Mn(II) + H^+$$

$$(CH_3)_3CC^{\cdot}O \longrightarrow (CH_3)_3C^{\cdot} + CO$$

$$(CH_3)_3C^{\cdot} + (CH_3)_3CCHO \longrightarrow (CH_3)_3CH + (CH_3)_3CC^{\cdot}O$$

$$(CH_3)_3C^{\cdot} + Mn(III) \longrightarrow Mn(II) + (CH_3)_3C^{+} \longrightarrow (CH_3)_2C{=}CH_2 + H^+$$

Scheme 3

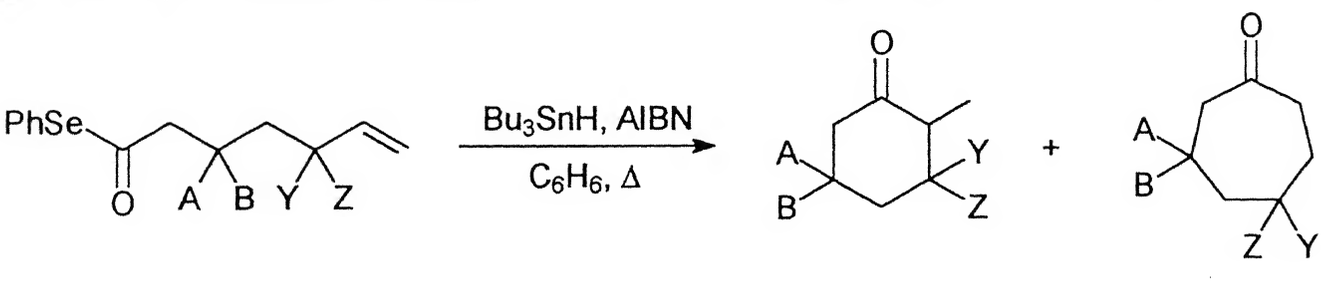
The acyl radical has been employed for the synthesis of ketones by radical chain addition of aldehydes to 1-alkenes in the presence of cobalt(III) acetate and dioxygen[8] (Eq. 2).

$$RCHO + CH_2 = CHR' \xrightarrow[O_2]{Co(II)} RCOCH_2CH_2R' \qquad \text{Eq. 2}$$

The generation and subsequent intermolecular reaction of acyl radical with alkenes have been recognized as an important method of carbon-carbon bond formation as reported by Kharasch[9] in 1949. The addition of acyl radical was subsequently extended to electron deficient alkenes[10-11] and this methodology has emerged as a very efficient route to the synthesis of functionalized ketones. The synthetic potential of the acyl radical as a fundamental functionalized free radical has renewed interest in the development of direct methods for its generation and recently a series of papers have described the ability of acyl cobalt salophen[12-14], phenyl selenolesters[15-18] and S-acyl xanthates[19] serving as acyl radical precursors. The acyl radical may be generated by an electron transfer process and it may involve either an outersphere or innersphere mode of electron transfer.

1.1.1 Tributyltin Hydride Mediated Radical Reactions

Crich and coworkers[17] have demonstrated that 6,7-unsaturated carbonyl radicals may be generated by the reaction of tributyl stannane with the corresponding selenolesters **1**. The later



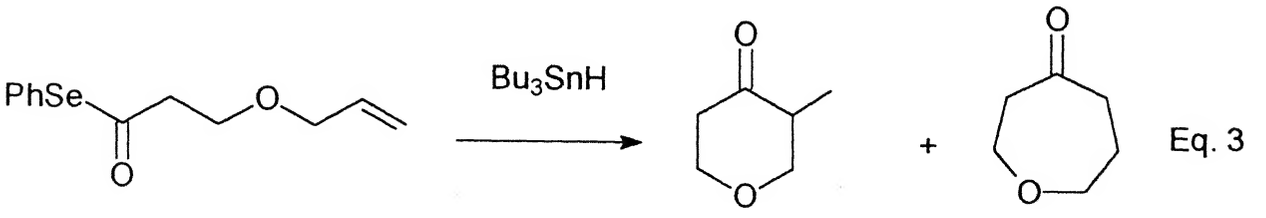
1 **2** **3**

(a). A = B = H, Y = OEt, Z = H	-	27%
(b). A----B = -CH_2CH_2O- , Y = OSi^tBuMe_2, Z = H	72%	24%

Scheme 4

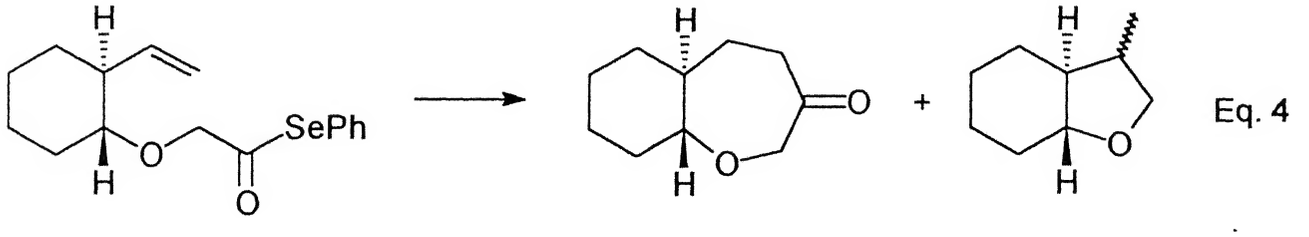
cyclized to give either cyclohexanones **2** or cycloheptanones **3** depending upon the nature and position of the substituents in hydrocarbon chain (Scheme 4).

Synthesis of six and seven membered heterocycles were carried out on irradiation with tri-n-butyl stannane, AIBN on the corresponding selenide. Thus, the allyl ether **4** gave under standard conditions six and seven membered heterocycles **5** and **6** respectively in 1:2 ratio (Eq. 3)[17].



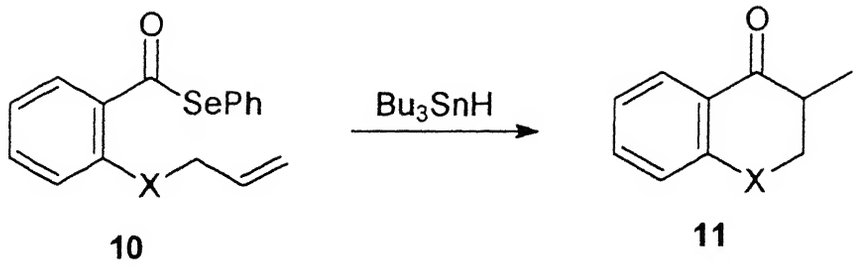
4 **5**(12) **6**(25)

The irradiation of cyclic selenolester **7** afforded a mixture of bicyclic compounds **8** and **9**, where the later product was obtained due to decarbonylation followed by 5-exo-trig cyclization. The formation of seven membered[20] ring in these reactions were rationalized due to kinetic cyclization in the exo-mode followed by rapid rearrangement to overall endo-mode cyclization (Eq. 4).



7 **8**(25) **9**(32)

A novel route was developed to 3-methyl chromanone **11a**, 3-methylthiochromanone **11b** and 2,3-dihydro-3-methylquinolin-4-one **11c** from salicylic acid **10a**, thiosalicylic acid **10b** and anthranilic acid **10c** respectively by carbonyl radical cyclization[21] (Scheme 5).

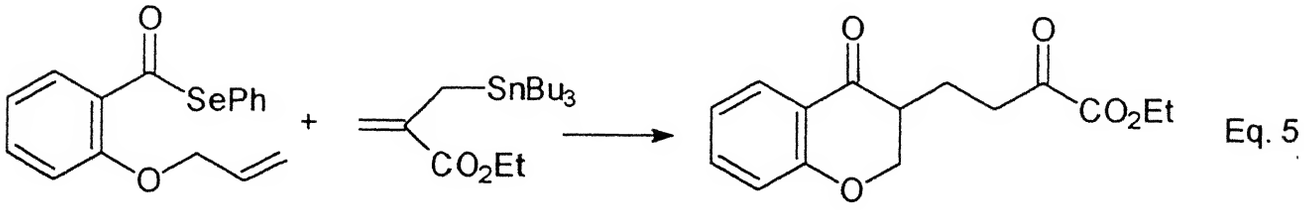


10 **11**

(a) X = O (a) 52%
(b) X = S (b) 66%
(c) X = N-Ac (c) 44%

Scheme 5

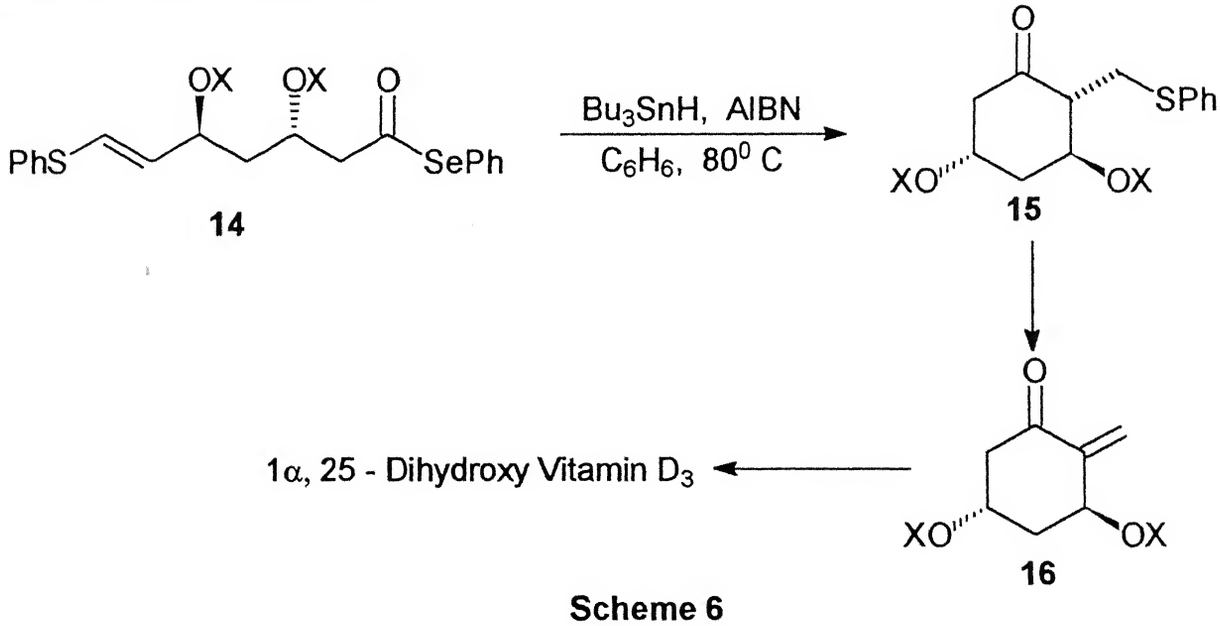
Chromanone **13** was synthesised from selenolester in one pot tandem radical cyclization/addition/β-elimination[22] sequence by using the activated allyl stannane **12** (Eq. 5).



Eq. 5

10a **12** **13**

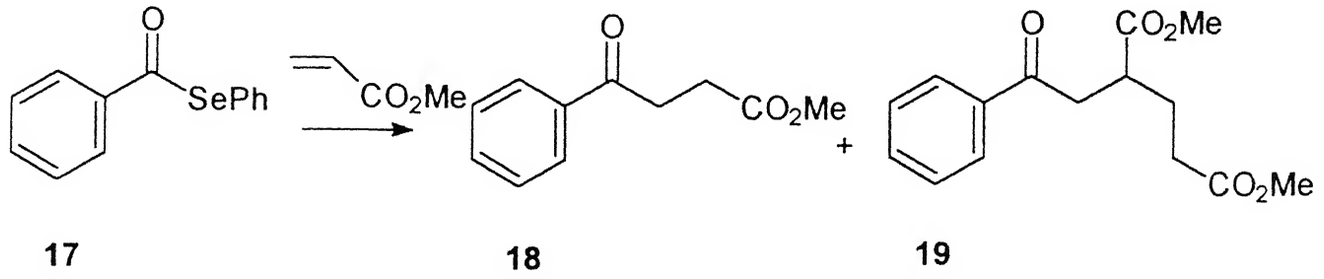
Acyl radical cyclization has been used as key ring forming step[23] during the synthesis of vitamin D_3 model (Scheme 6).



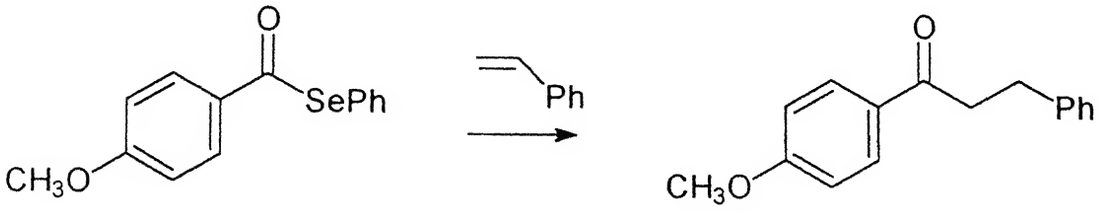
14 **15** **16**

Scheme 6

Similarly, Boger and coworkers have demonstrated that acyl radicals generated from the substituted aryl and phenyl selenolesters **17** and **20** in the presence of electron deficient alkenes provided high yields of the intermolecular alkene addition products **18**, **19** and **21** (Scheme 7)[24].



17 **18** **19**

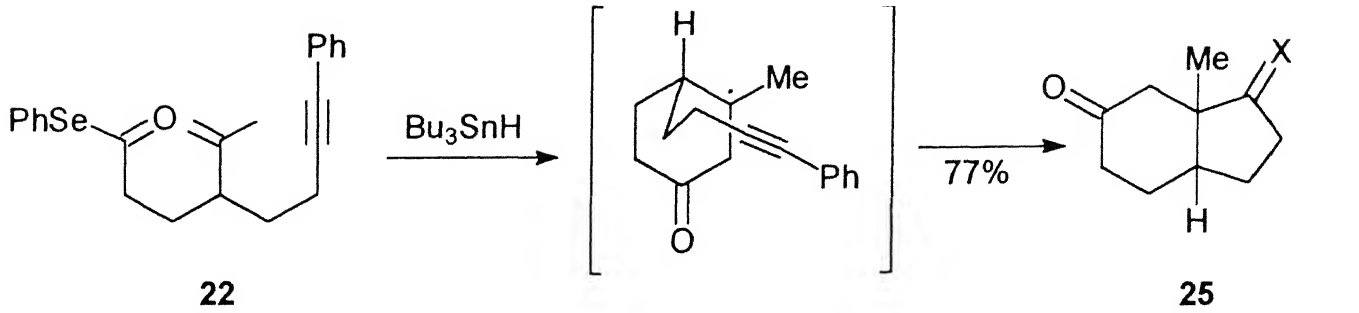


20 **21**(71)

Scheme 7

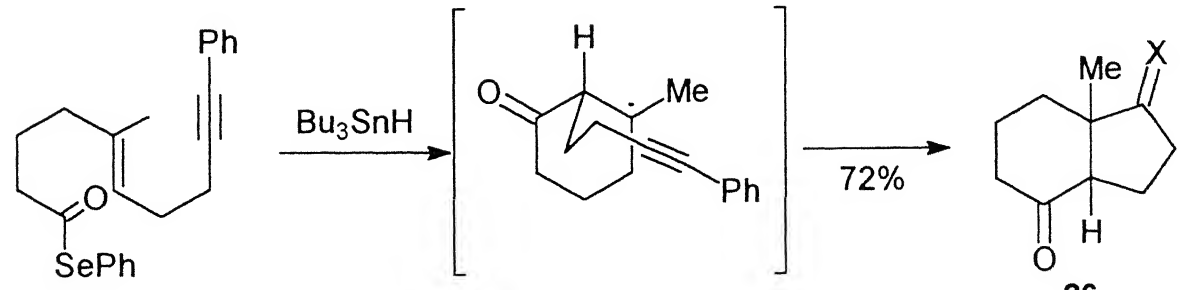
Subsequently, they have also reported that aryl radicals can be generated[25] from phenyl selenolesters which can undergo a tandem free radical alkene addition including intramolecular polycyclization reactions. Thus, they demonstrated the tandem cyclization initiated with the generation of acyl radicals from **22-24** followed by sequential[26,27] 6-endo-trig/5-exo-dig, 6-endo-trig/6-exo-dig, or 6-endo-trig/6-exo-trig free radical cyclization provided **25-27** respectively (Scheme 8).

In each instance, the polycyclization reaction[25] was initiated with clean 6-endo-trig versus 5-exo-trig free radical cyclization that may be attributed to the extent of substitution at the proximal alkene. They have also carried out cyclization followed by intermolecular addition using electron deficient alkenes (Scheme 9).



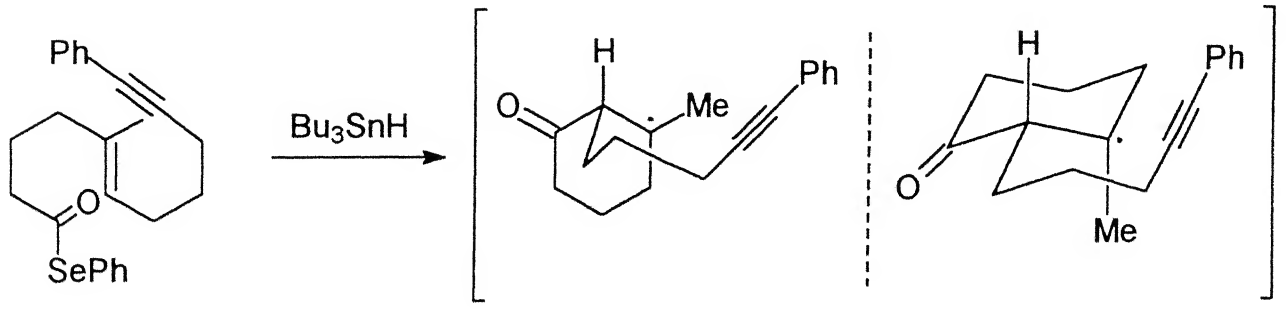
22 **25**

O_3, Me_2S
68%
- X=CHPh (> 98% cis)
- X=O (>98% cis)



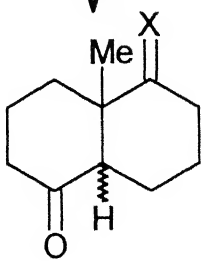
23 **26**

O_3, Me_2S
74%
- X = CHPh (>97% cis)
- X = O (>96% cis)



24

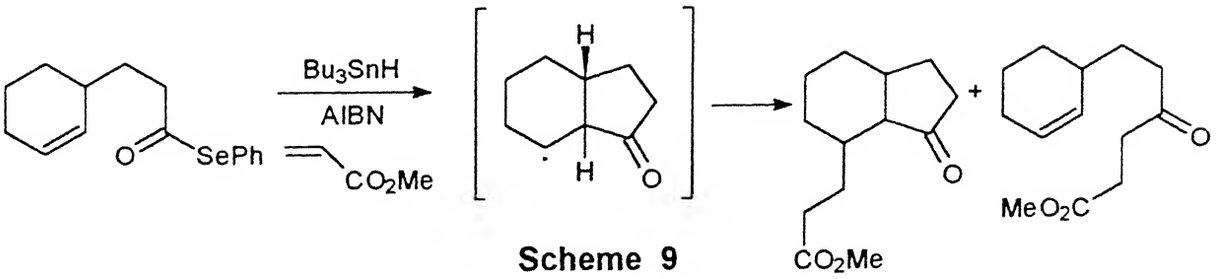
82%



27

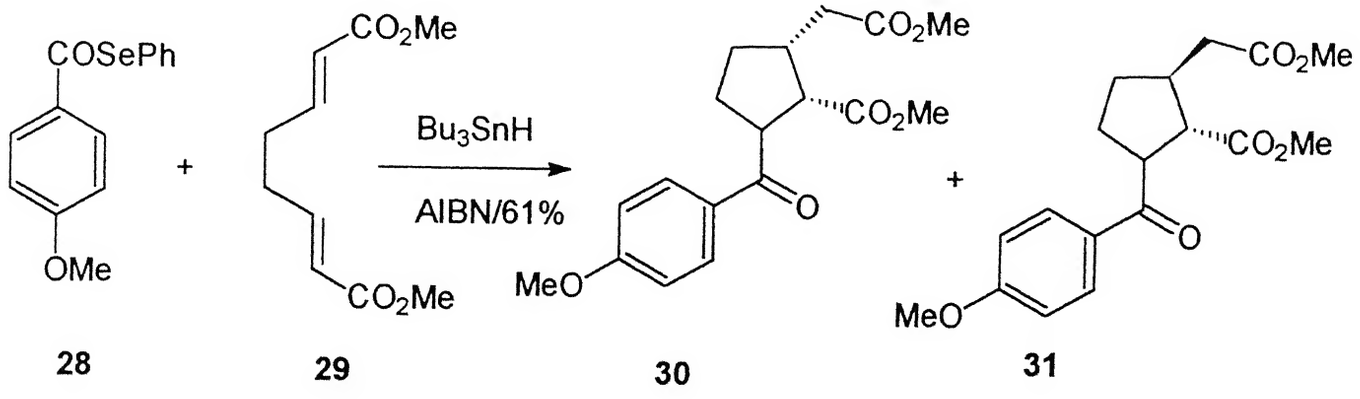
O_3, Me_2S
85%
- X = CHPh (58:42 cis:trans)
- X = O (58:42 cis:trans)

Scheme 8



Scheme 9

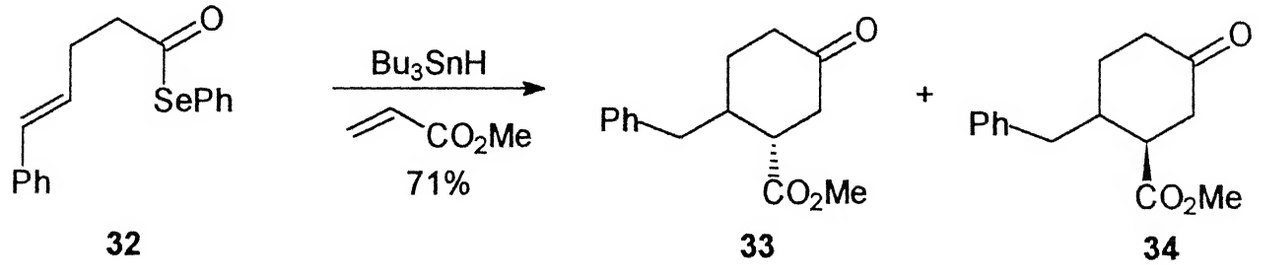
Conversely, they have also carried out[25] the intermolecular addition followed by cyclization reaction[28] as evidenced by the reaction between phenylselenolesters **28** in the presence of the acceptor alkene **29** possessing pendent proximal alkene which proceeded with intermolecular acyl radical alkene addition, intramolecular 5-exo-trig free radical alkene cyclization (Scheme 10).



28 **29** **30** **31**

Scheme 10

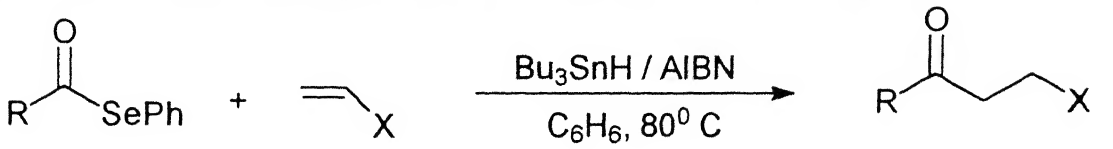
A complementary tandem addition cyclization reaction[25] was carried out by the treatment of acyl radical precursor with tributyltinhydride in the presence of methyl acrylate to give the cyclohexanones **33** and **34** in good yields (Scheme 11).

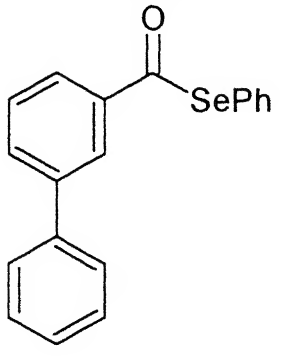
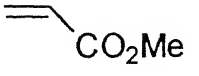
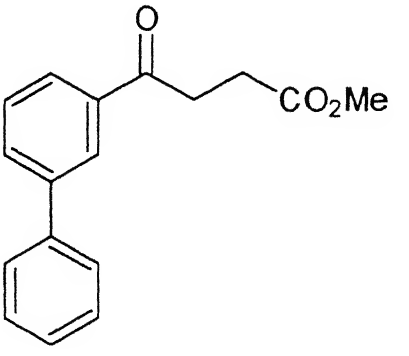
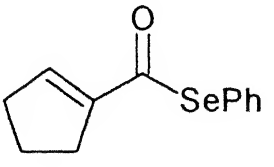
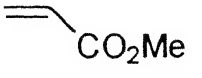
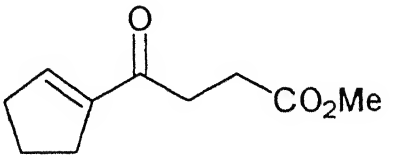
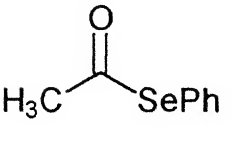
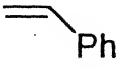
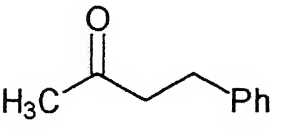
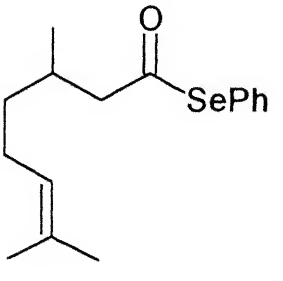
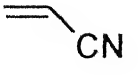
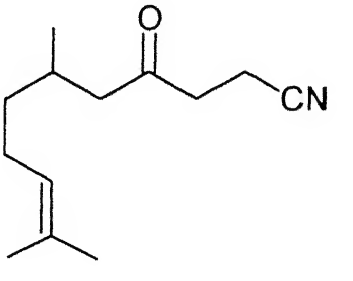
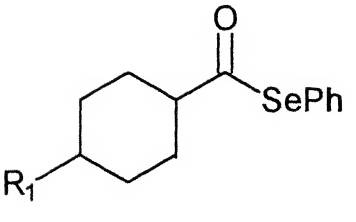
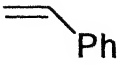
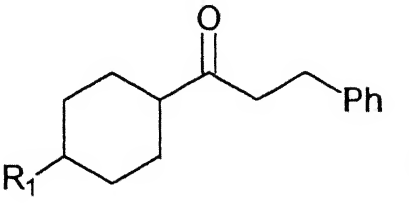


32 **33** **34**

Scheme 11

Table 1. Intramolecular Acyl Radical-Alkene Addition Reactions

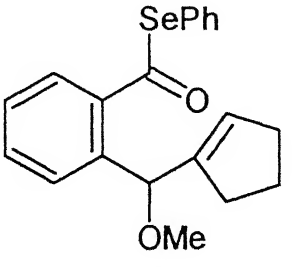
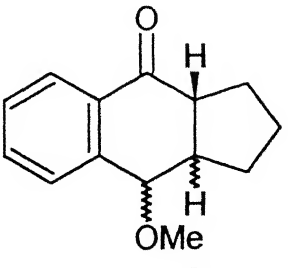
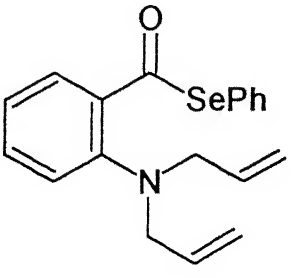
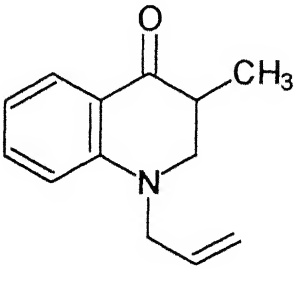
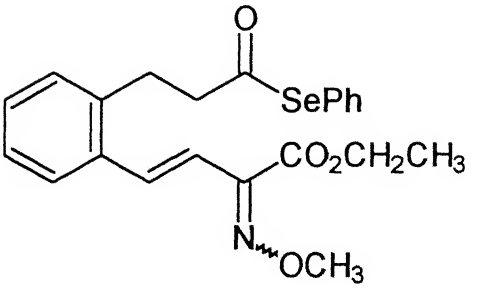
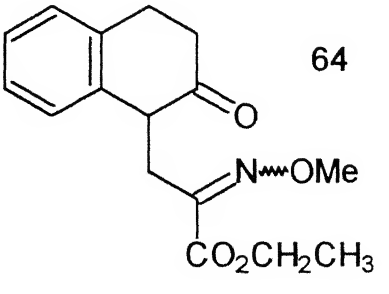


Entry	Phenylselenoester	Alkene	Product	Yield %
1				62
2				68
3				51
4				51
5				45

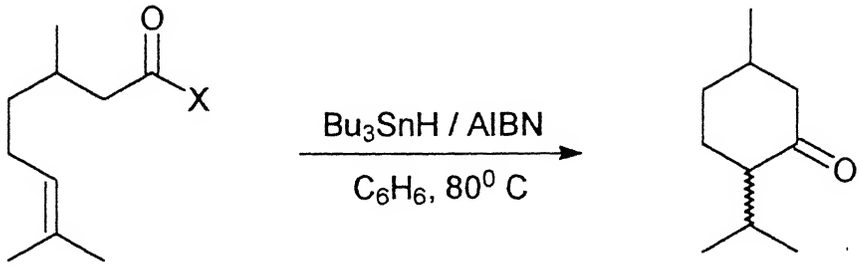
Recently, it has been reported that primary alkyl-, vinyl- and aryl substituted acyl radicals generated by tributyltinhydride treatment of the corresponding phenyl selenolesters participate cleanly in intermolecular addition reactions with alkenes bearing electron withdrawing or radical stabilizing substituents (Table 1)[29].

Similarly, the intramolecular alkene addition reactions of the acyl radicals generated from phenylselenolesters proceed efficiently, with little or no competitive reduction or decarbonylation (Table 2)[30].

Table 2. Generation and Intramolecular Free- Radical Cyclization of Acyl Radicals

Entry	Phenylselenoester	Product	Yield (%)
1			86
2			69
3			64

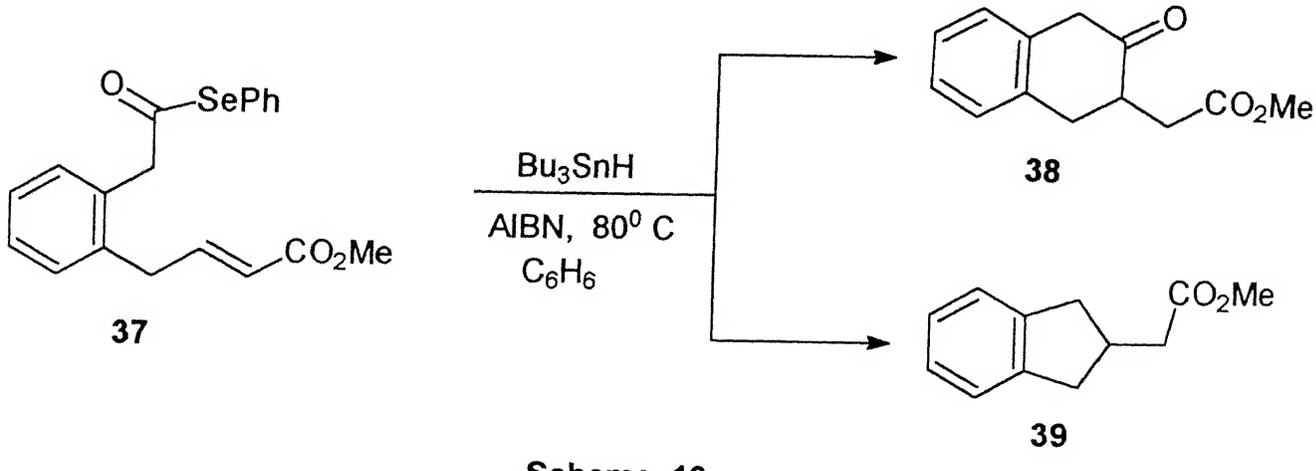
Acyl radicals generated from phenyl selenolesters proceed more effectively than the corresponding reactions employing acyl chlorides or phenyl thioesters as precursors (Scheme 12)[31].



35	**36**
X = SePh(**a**)	84
X = SPh(**b**)	no reaction
X = Cl(**c**)	59

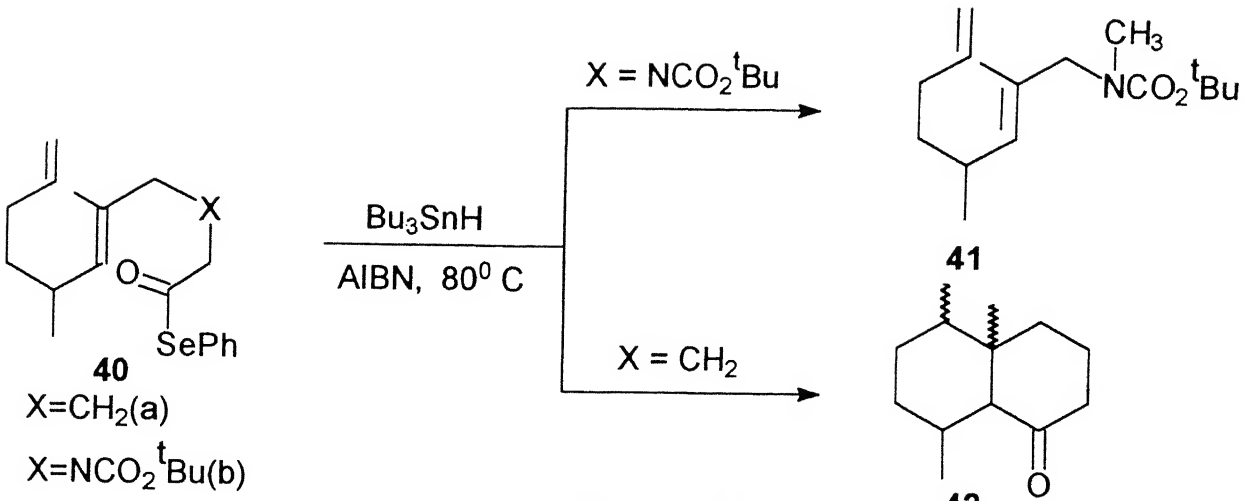
Scheme 12

They have also described decarbonylation versus cyclization as the intramolecular 6-exo-trig cyclization of an acyl radical with an activated acrylate acceptor proceeds at a near identical rate to decarbonylation of a benzylic acyl radical (Scheme 13)[31].



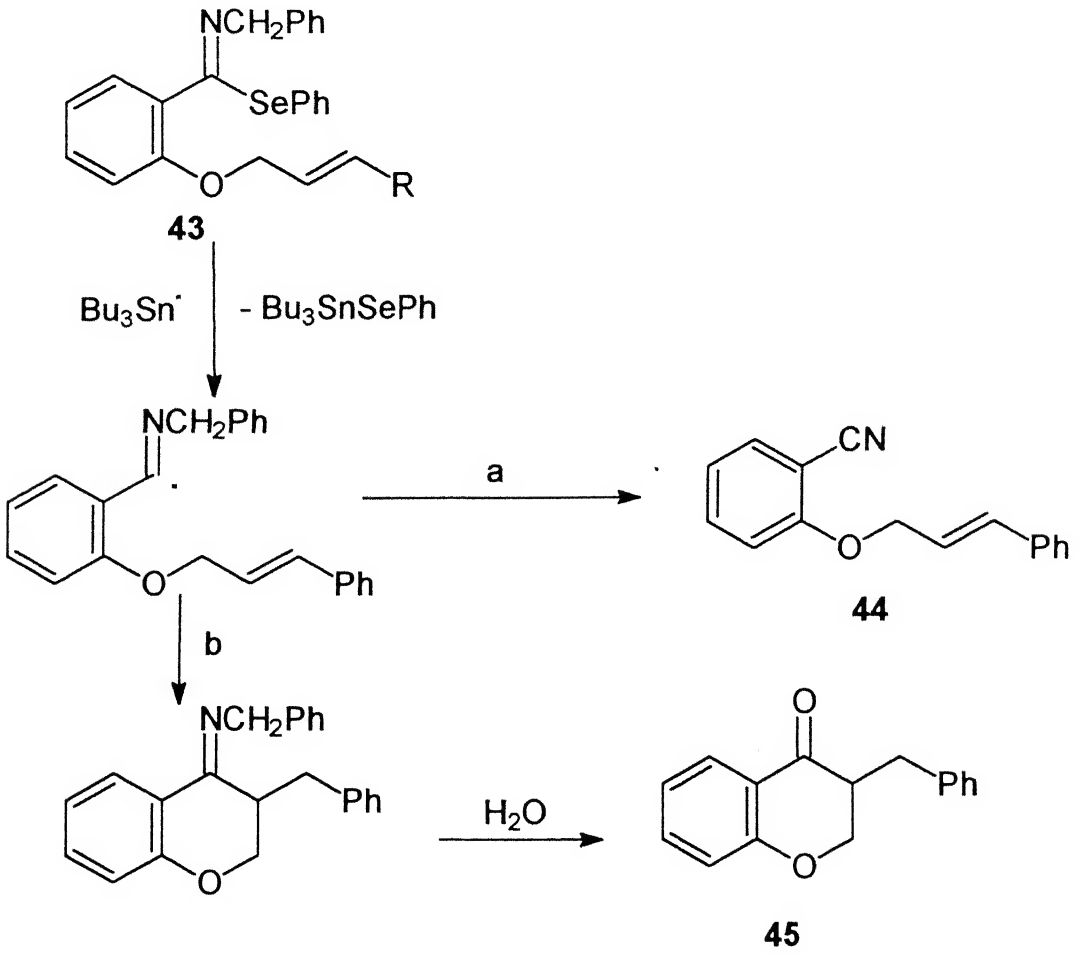
Scheme 13

Similarly, 6-endo-trig cyclization of the primary acyl radical generated from **40a** proceeds without competitive decarbonylation, the decarbonylation reaction of acyl radical derived from **40b** to provide the heteroatom-stabilized[31] primary radical precluded the formation of 6-endo-trig-cyclization **42** (Scheme 14).



Scheme 14

Thus, the rate of 6-endo-trig cyclization of primary acyl radicals with unactivated alkenes proved to be slower than decarbonylation of α-heteroatom-substituted acyl radicals.

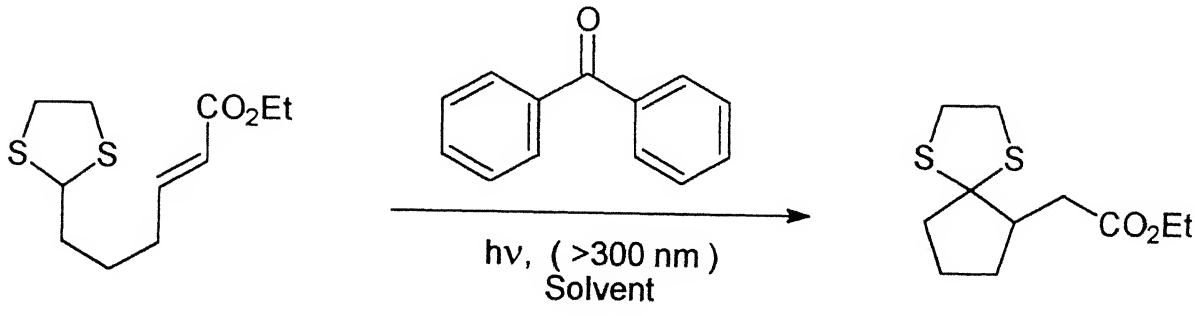


Scheme 15

Bachi and coworkers[32] have described the employment of imidoyl radicals, as intermediates in the synthesis of cyclic ketones and polyheterocyclic compounds. In this transformation the imidoyl radical acts as a synthetic equivalent to the carbonyl radical (Scheme 15).

1.1.2 Photochemical Reactions

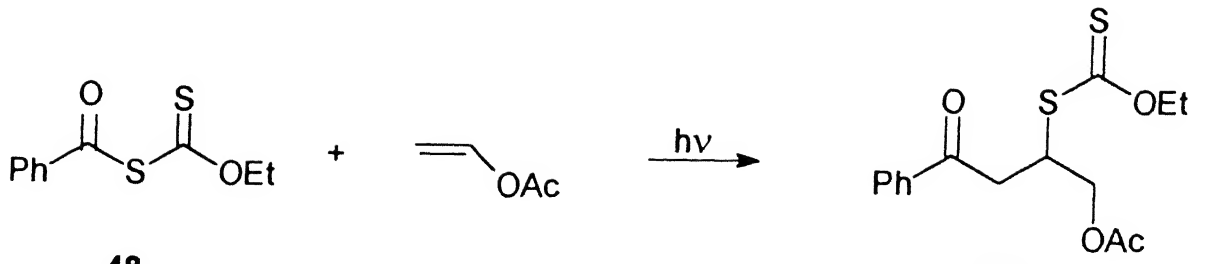
Dithioacetal was found to be a good radical generating group[33] in the presence of photo-exited benzophenone and the resulting radical could be trapped in the intramolecular manner to give cyclopentanone derivatives (Scheme 16).



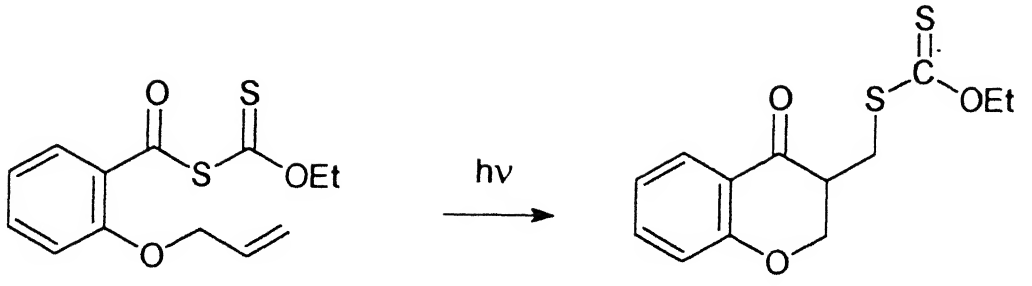
46 **47**

Scheme 16

Zard and coworkers have developed S-acyl xanthates[34] as a precursor for acyl radical. A pioneering investigation of Barton and coworkers[35] revealed that irradiation with visible or UV light on xanthates result into the formation of acyl radicals. Thus, benzoyl derivative **48** was first prepared from benzoyl chloride and potassium-O-ethyl xanthate, on irradiation with 250W tungsten lamp in a refluxing mixture of toluene and allyl acetate lead to the adduct **49** in good yield. The intramolecular version of this reaction was also performed from the salicylic acid derivative **50** to afford the chromanone **51** in 70% yield (Scheme 17)[19].



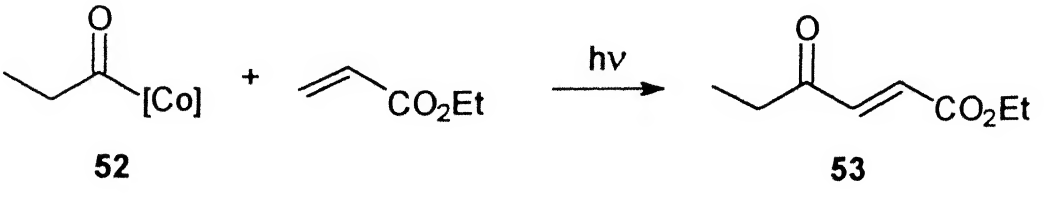
48 49



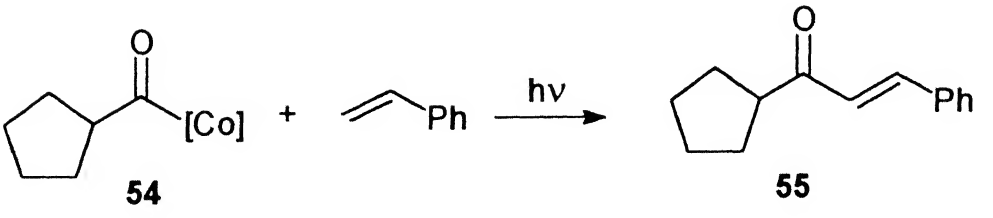
50 Scheme 17 51

1.1.3 Cobalt Mediated Radical Reactions

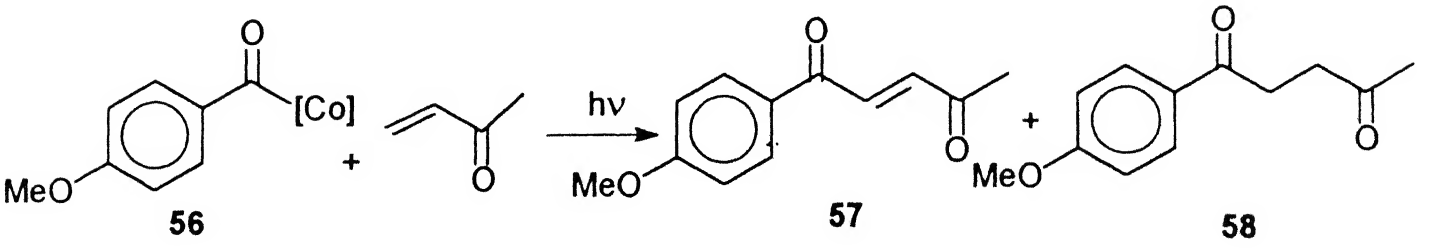
Pattenden and coworkers have reported a range of acyl cobalt salophen reagent precursors to the corresponding acyl radicals. Irradiation of de-aerated, refluxing solution of the acylcobalt salophen **52**, **54**, **56** and **59** in dichloromethane in the presence of activated carbon-carbon double bonds led to the corresponding[13-14] functionalised alkenes **53**, **55**, **57**, **58** and **60** in good yields (Scheme 18).



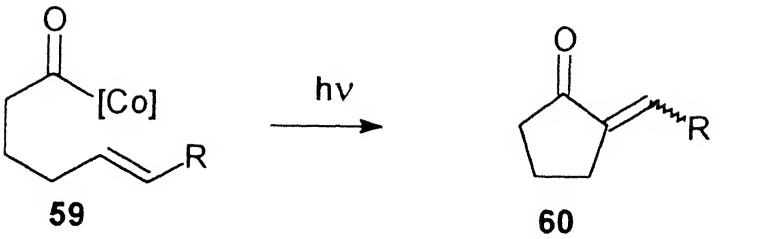
52 53



54 55



56 57 58

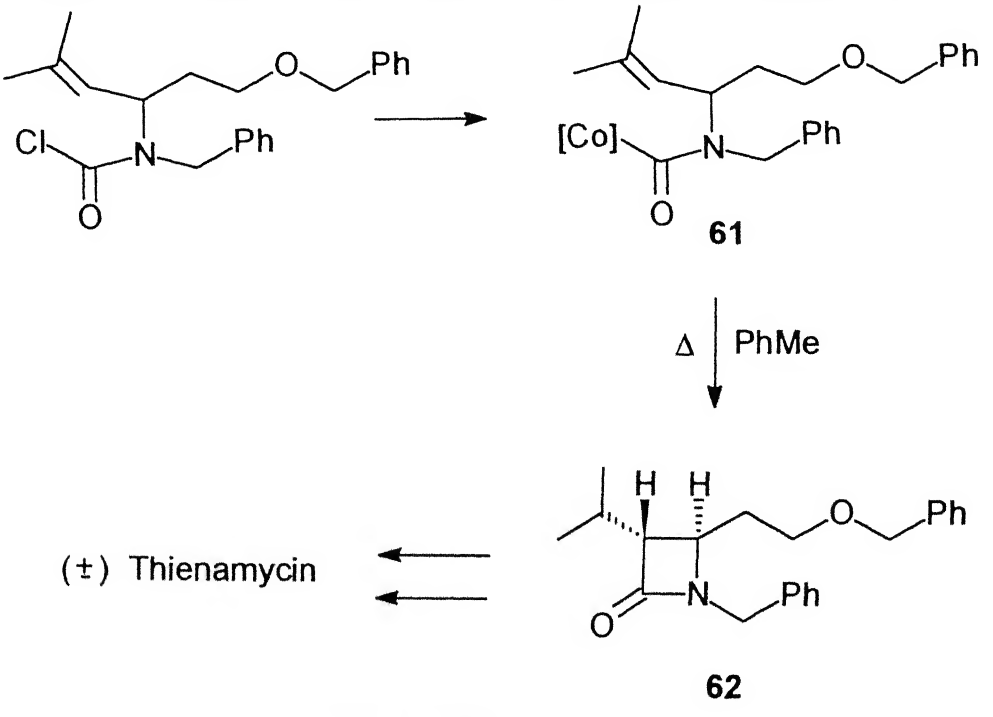


59 **60**

(a) R = Ph
(b) R = CO_2Et

Scheme 18

The key intermediate[36] **62** for the synthesis of (±)-thienamycin has been prepared by heating a solution of carbamyl cobalt salophen **61** in toluene (Scheme 19).

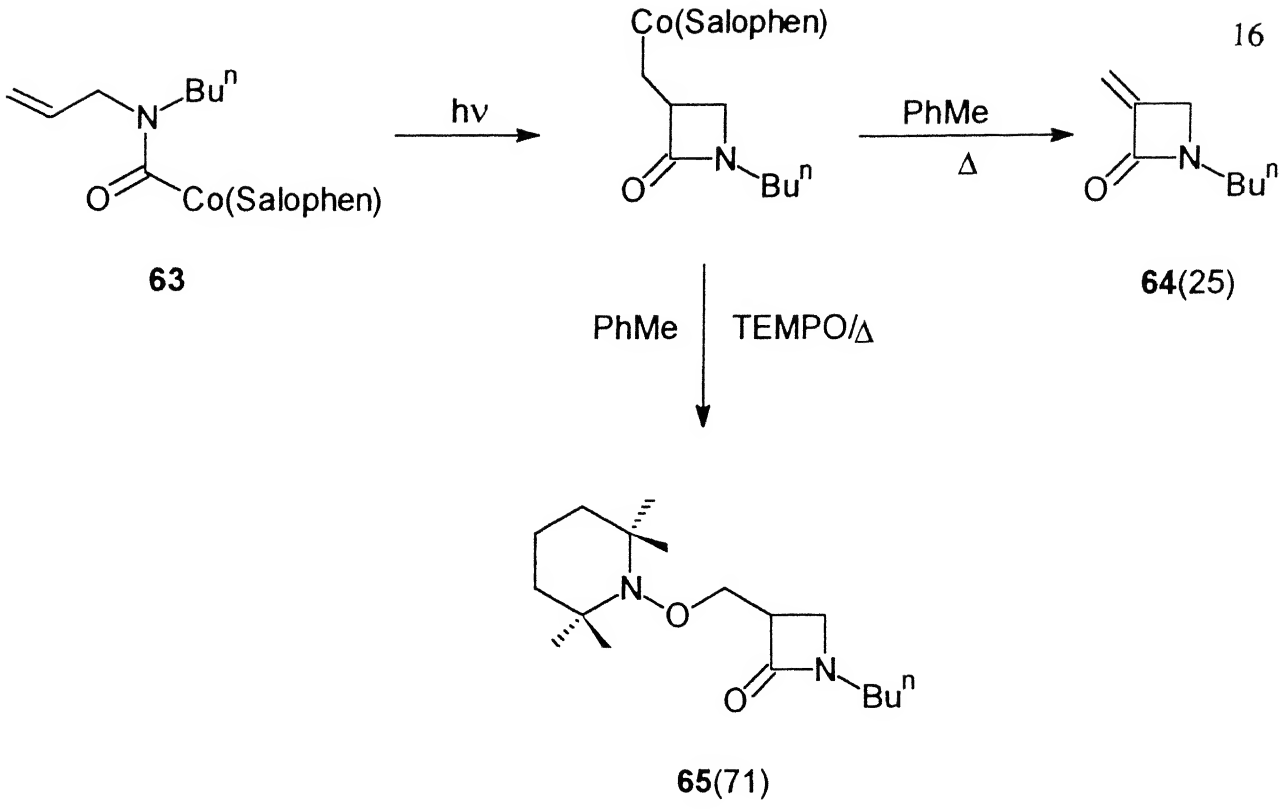


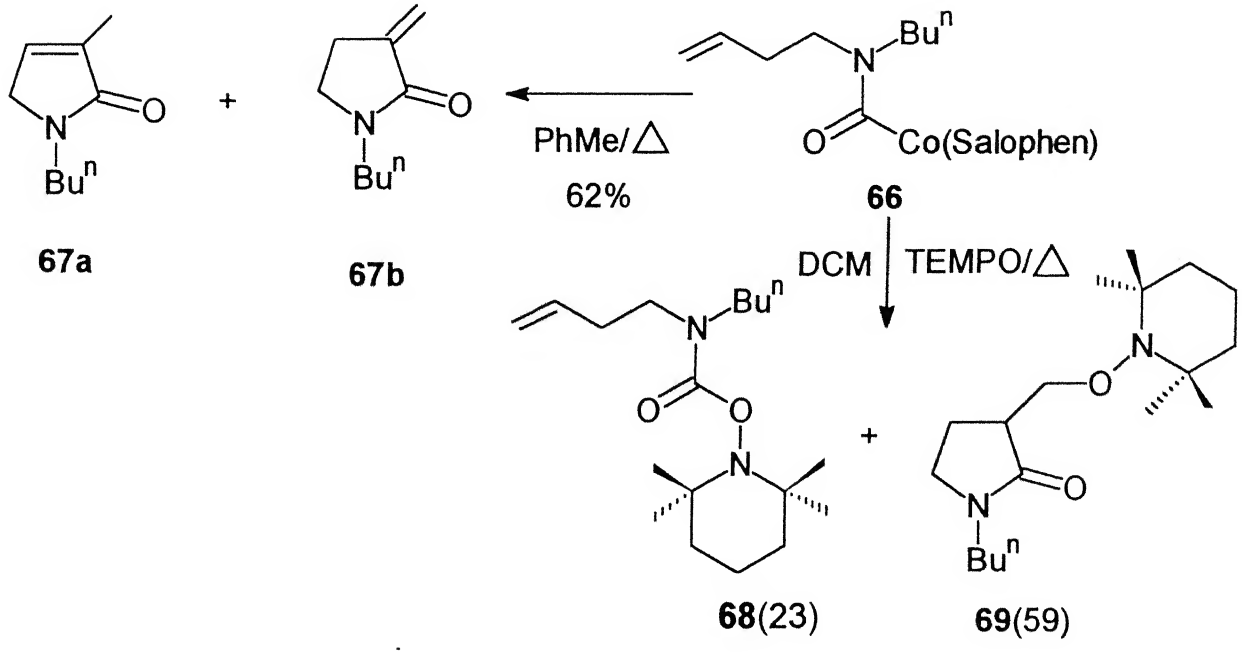
61 **62**

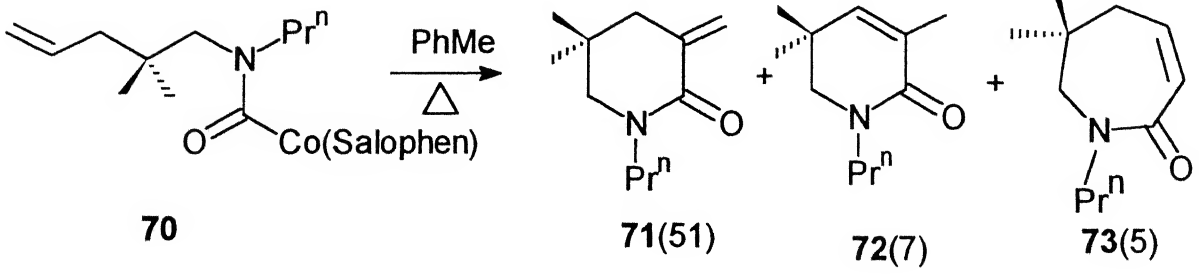
Scheme 19

These workers have also shown that unsaturated carbonyl cobalt salophens **63**, **66** and **70** undergo homolytic cleavage producing carbamyl radicals, which then undergo cyclization, followed by trapping or dehydrocobaltation leading to β-, γ- and δ-lactams **64**, **65**, **67-69**, **71-73** (Scheme 20)[37].

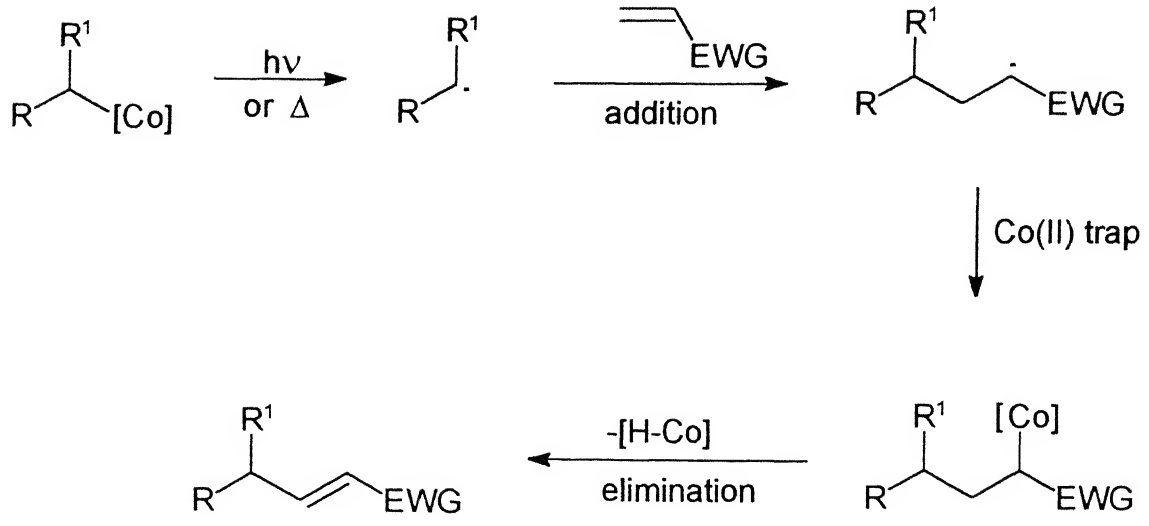
The mechanism for the radical addition-elimination, promoted by acyl cobalt reagent, can be explained by Michael addition followed by dehydrocobaltation (Scheme 21).


Co(Salophen)
Bu^n
hν
PhMe
Δ
Co(Salophen)
63
64(25)
PhMe
TEMPO/Δ
65(71)


Bu^n
PhMe/△
62%
Co(Salophen)
66
67a
67b
DCM
TEMPO/△
68(23)
69(59)


Pr^n
PhMe
△
Co(Salophen)
70
71(51)
72(7)
73(5)

Scheme 20



Scheme 21

1.1.4 Epoxidation of Alkenes in the Presence of Dioxygen

The selective monooxygenation of various organic compounds utilizing dioxygen is one of the challenging tasks in synthetic organic chemistry. Recently, much efforts have been made toward monooxygenation reactions of alkenes via single oxygen atom transfer by combined use of dioxygen and various organic reducing agents. For example, aerobic oxygenation of alkenes into the corresponding alcohols by using cobalt(II) Schiff base complexes in ethanol was reported[38,39]. In the similar oxidation system, terminal alkenes were also converted into the corresponding methyl ketones[40]. Further, a new method for the selective hydration of alkenes under neutral conditions was established by combined use of dioxygen and 2-propanol, a reductant, using bis(1,3-diketonato) cobalt(II) complex as a catalyst[41].

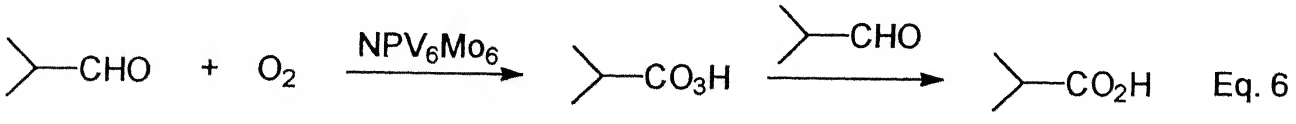
Of various monooxygenated compounds derived from alkenes, epoxides are regarded as one of the most useful synthetic intermediates and many trials have thus been reported. Epoxides are generally prepared from the corresponding alkenes by using peroxy compounds, such as m-chloroperbenzoic acid or peracetic acid. These reagents are converted into the

corresponding carboxylic acids as coproducts during epoxidation of alkenes. The storage and shipping of peracids press serious restrictions on its use in large scale. On the other hand, epoxidation with molecular oxygen as an oxidant is very useful and promising synthetic method. Several epoxidation systems of alkenes have recently been reported using metal catalysts.

1.1.4.1 Molybdenum and Vanadium Catalysts

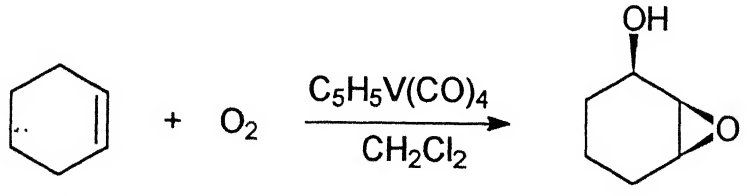
Alkenes were epoxidised with dioxygen in the presence of two equivalents of 2-methylpropanal under the influence of a catalytic amount of mixed heteropolyoxometalate NPV_6Mo_6 to give the corresponding epoxides in moderate to good yields (Table 3)[42].

Aliphatic aldehydes bearing di-or tri alkyl groups on the α-position of the carbonyl carbon epoxidise cleanly with good selectivity. However, no epoxide was obtained when n-butanal and benzaldehyde were employed as reducing agents. In the absence of alkene, aldehyde oxidized to the corresponding carboxylic acid(Eq. 6)[42]



Eq. 6

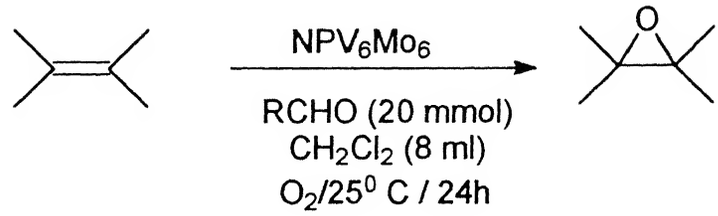
Epoxides can also be formed from the oxidation of alkenes by dioxygen via in *situ* generation of hydroperoxides by autoxidation. An interesting example is the direct stereoselective oxidation of cyclohexene **74** by dioxygen to syn-1,2-epoxycyclohexan-3-ol **75** catalyzed by $CpV(CO)_4$ with a 65% yield and ~99% stereoselectivity (Eq. 7)[43].

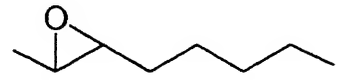
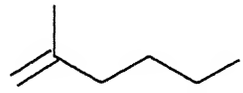
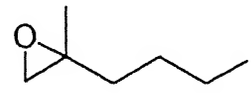
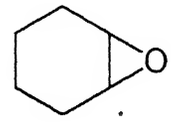
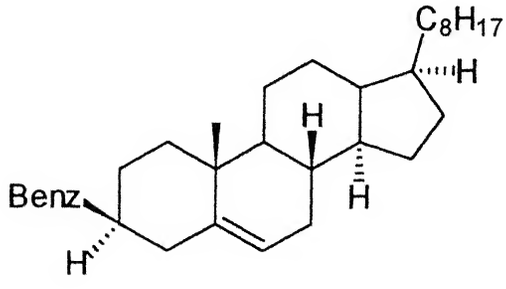
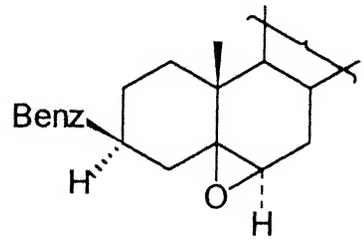
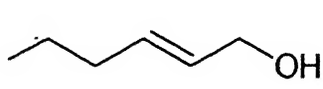
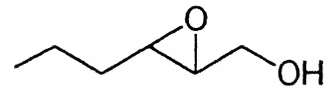
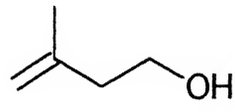
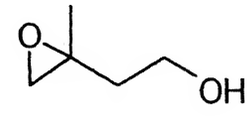


Eq. 7

74 **75**

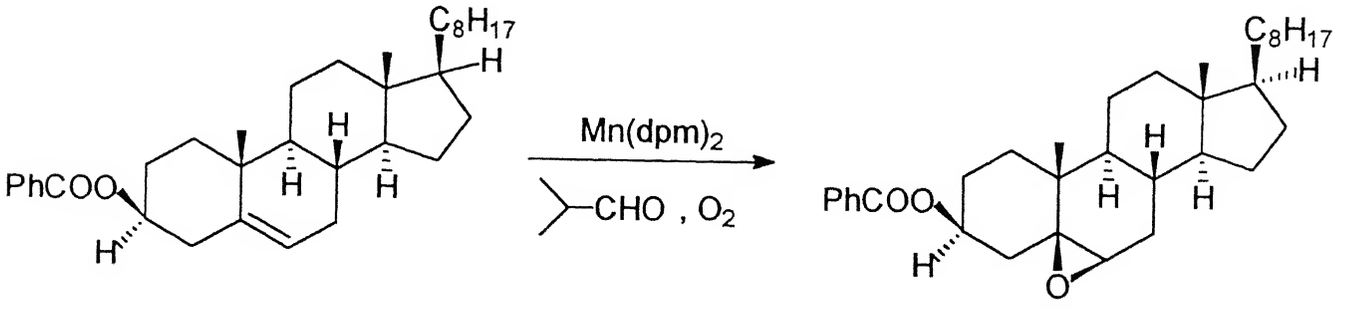
Table 3. Epoxidation of Alkenes with Dioxygen and Isobutanal



Entry	Substrate	Product	Conversion %	Yield(select) % (cis / trans)
1			66	59(89) (99/1)
2			100	89(89)
3			83	78(94)
4			82	82(100) (40/60)
5			96	67(70)
6			94	92(98)

1.1.4.2Manganese

In the presence of a catalytic amount of bis(dipivaloylmethanato)manganese(II) various cholesterol derivatives are smoothly transformed to their corresponding β-epoxides in good to high yields with combined use of dioxygen and isobutanal (Scheme 22)[44]. This stereoselectivity is the reversal to that of the cases using peracid such as m-chloroperbenzoic acid.



76

β–*epoxide*

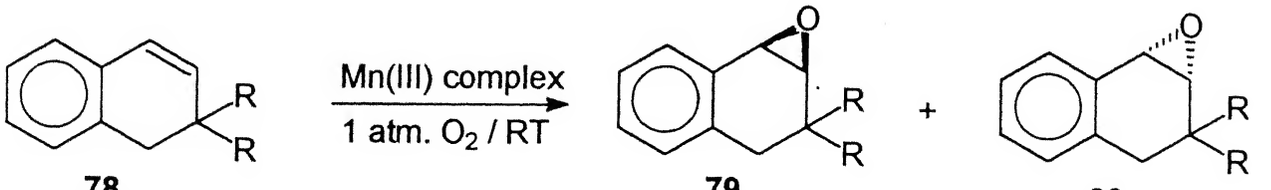
77

Hdpm = ^{t}Bu ^{t}Bu

Scheme 22

Enantioselective epoxidation of unfunctionalised alkenes with combined use of dioxygen and pivalaldehyde was demonstrated in the presence of a catalytic amount of optically active manganese(III) salen complexes (Table 4)[45].

Table 4. Asymmetric Epoxidation of 1,2-Dihydronapthalenes



78

79

(1R, 2S)-(+)

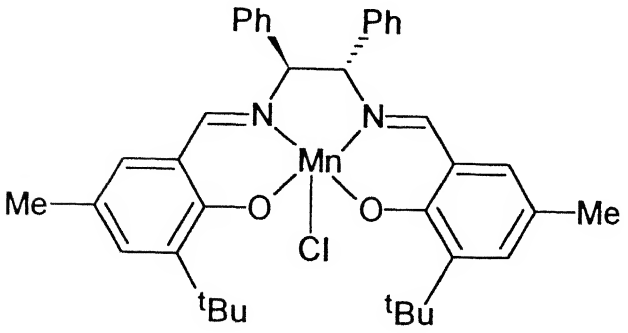
80

(1S,2R)-(-)

1 : R = H
2 : R = CH_3

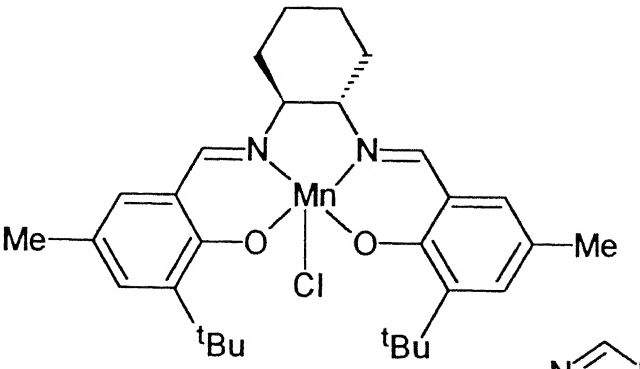
Entry	Catalyst	Alkene	Additive	Yield %	Optical yield %ee	
					(1R,2S)-(+)	(1S,2R)-(-)
1	A	1	-	42	12	-
2	A	2	-	51	6	-

3	**B**	**1**	-	37	6	-
4	**A**	**1**	N-Me-Imd	62	-	52
5	**A**	**2**	N-Me-Imd	67	-	56
6	**B**	**1**	N-Me-Imd	78	-	63
7	**B**	**2**	N-Me-Imd	67	-	72



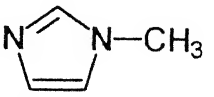
81

A (S,S)-Ph-Salen-Cl



82

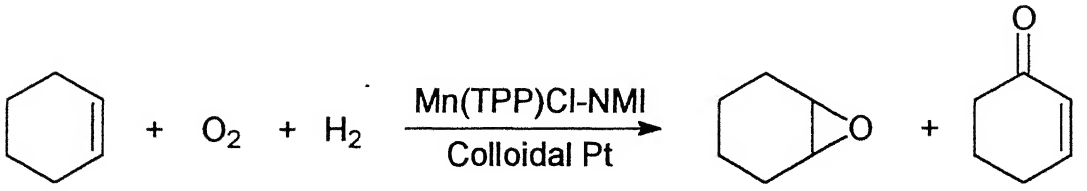
B (S,S)-Cyclo-Salen-Cl



N-Me-Imd

Dihydronaphthalene derivatives were converted into the corresponding optically active epoxides in good yields with 60-77% enantiomeric excess (Table 5).

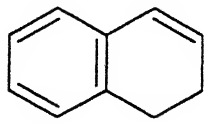
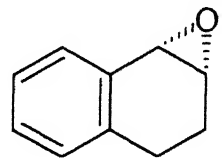
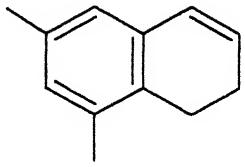
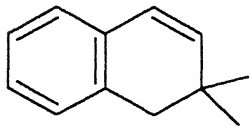
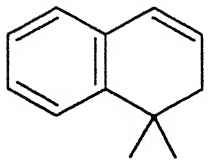
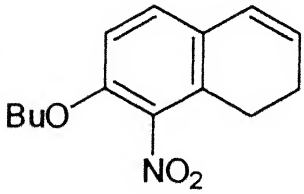
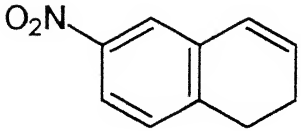
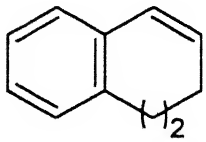
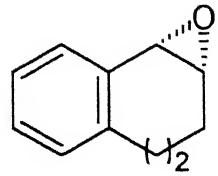
Tabushi and coworkers have reported that oxygenation of cyclohexene **74** in the presence of Mn(TPP)Cl, 1-methylimidazole(NMI), dioxygen and (H_2 + colloidal platinum) produced cyclohexene oxide **83** in good yield (Eq. 8)[46].



74 **83**(92) **84**(6) Eq. 8

Although, a substantial amount of water was directly produced from the reaction of dioxygen and hydrogen, epoxide was catalytically formed with respect to manganese (65 turn

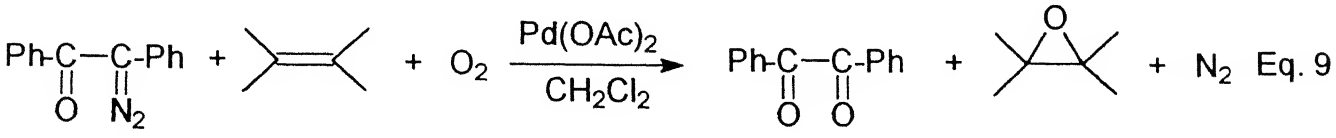
Table 5. Examples of Asymmetric Epoxidation

Entry	alkene	yield %	optical yield %ee	note
1		78	63	 (1S,2R)
2		73	72	
3		80	63	
4		35	63	
5		38	66	
6		43	43	
7		52	77	 (1S,2R)

overs) and platinum (300 turnovers). The reactivity order of alkenes was found to be similar to that observed with a related Mn(TPP)Cl/PhIO catalytic epoxidation system. In contrast to this PhIO system, the epoxidation of alkenes with dioxygen and hydrogen proceeds with retention of configuration.

1.1.4.3 Palladium

Ryang and coworkers have reported the epoxidation of alkenes using azobenzil **85** in the presence of molecular oxygen and catalytic amount of $Pd(OAc)_2$ (Eq. 9)[47].

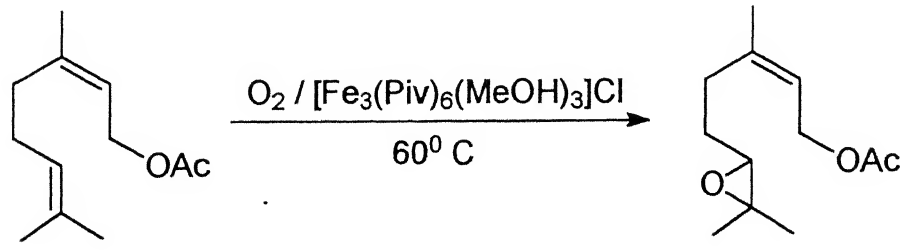


Eq. 9

85 **86**

1.1.4.4 Iron

3-Oxotriiron complexes $[Fe_3O(RCO_2)_6L_3]X$ [R=Me, Bu^t(piv); L=MeOH, Py; X=Cl, OAc] have recently been shown to catalyse the epoxidation of alkenyl acetate by dioxygen under mild conditions (60° C, 1 atm) (Eq. 10)[48].



Eq. 10

87 **88**(87)

The regiospecificity of this reaction resembles that of peracid epoxidation but is opposite to that of Bu^{t}OOH/$VO(acac)_2$. Alkenyl acetates can be efficiently epoxidized using this reagent

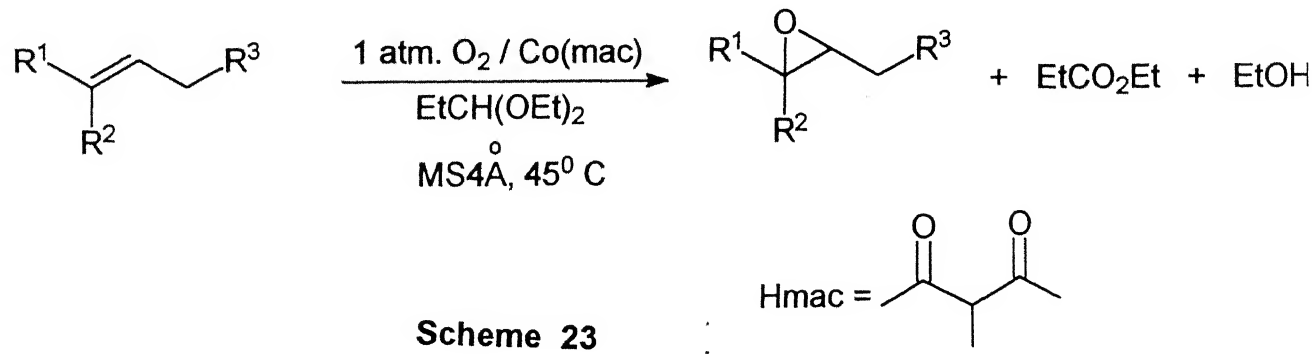
as compared to simple alkenes. One mole of dioxygen was consumed for per mole of epoxide produced. This is twice the amount required for the stoichiometry of the reaction, and the detected oxidative degradation products account for one oxygen atom of O_2 not found in the epoxide product.

1.1.4.5 Ruthenium

Epoxidation of cholesteryl acetate with air in the presence of a catalytic amount of dioxo(tetramesitylporphyrinato)ruthenium(VI) furnishes in 85% yield a 99:1 mixture of the epoxides (β:α)[49].

1.1.4.6 Cobalt

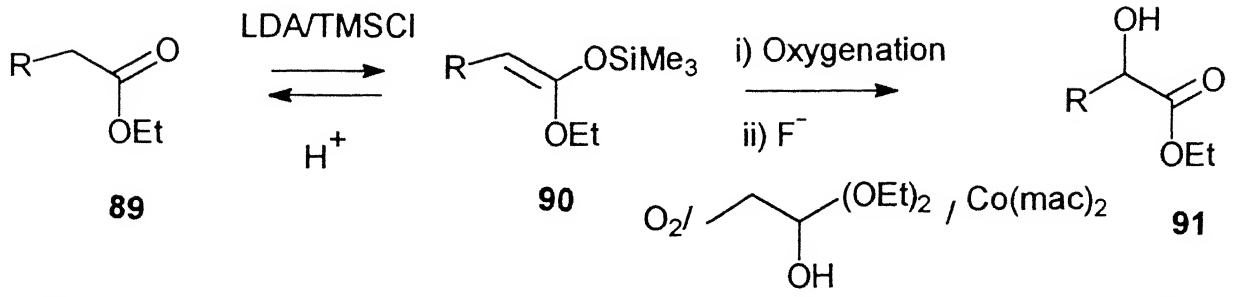
Mukaiyama and coworkers have reported that cobalt(II) complex catalyses epoxidation of various trisubstituted alkenes in the presence of diethyl acetal and dioxygen under neutral conditions (Scheme 23)[50].



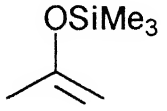
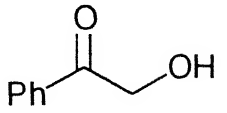
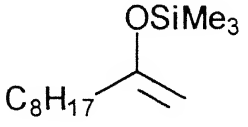
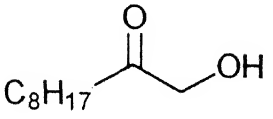
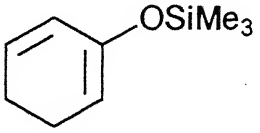
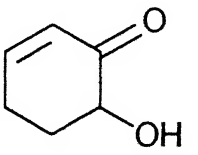
Scheme 23

Various silylenol ethers and silylketone acetal were also smoothly monooxygenated into the corresponding α-hydroxy carbonyl compounds (Table 6).[51]

Table 6. Monooxygenation of Silylenol Ethers



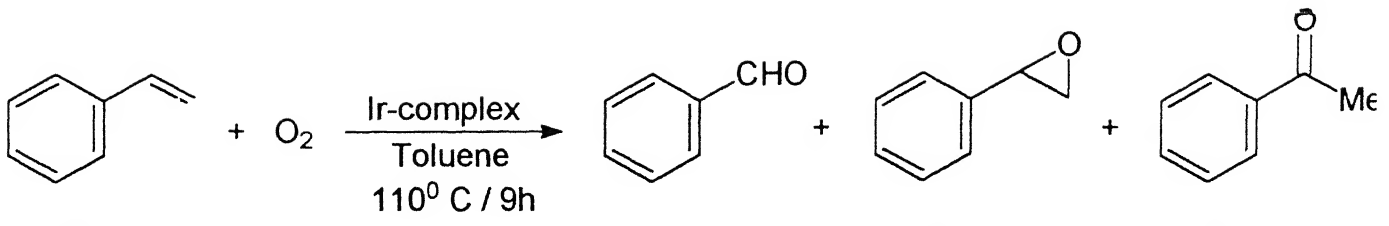
89 **90** **91**

Entry	Alkene	Time/h	Product	Yield(%)
1		9		83
2		10		77
3		10		87

Recently, in our laboratory reported that cobalt(II) complex efficiently catalyses the reaction of trisubstituted alkenes in the presence of 2-methylpropanal and dioxygen to give the corresponding monoepoxide in very good yield.[52]

1.1.4.7 Iridium

Takao and coworkers have studied iridium complex catalyzed oxidation reaction of styrene **92** and triphenylphosphine. The Vaska complex $XIr(CO)(PPh_3)_2$ and the biphosphine chelate complex have been found to be effective as oxidation catalysts. These workers have also employed palladium salts as catalyst for the sake of comparison (Scheme 24)[53].

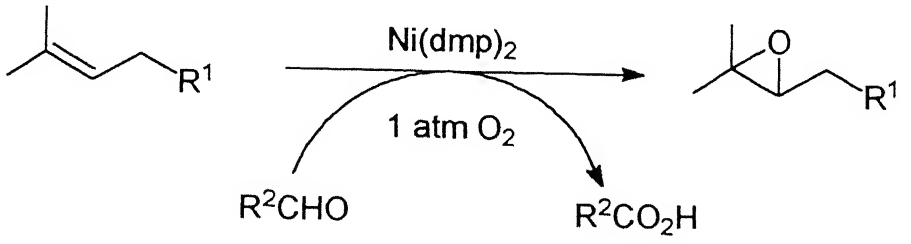


92 **93** **94** **95**

Scheme 24

1.1.4.8 Nickel

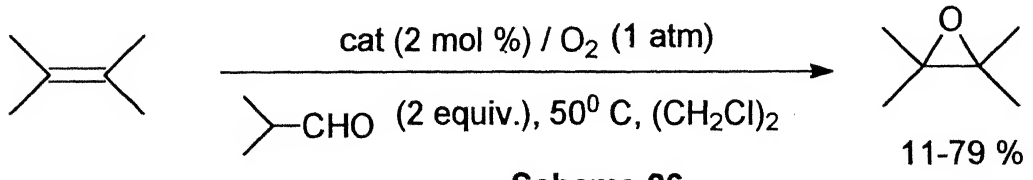
Several studies have been reported for the epoxidation of alkenes using $Ni(dmp)_2$ catalyst in the presence of dioxygen and several aldehydes at room temperature (Scheme 25)[54].



Scheme 25

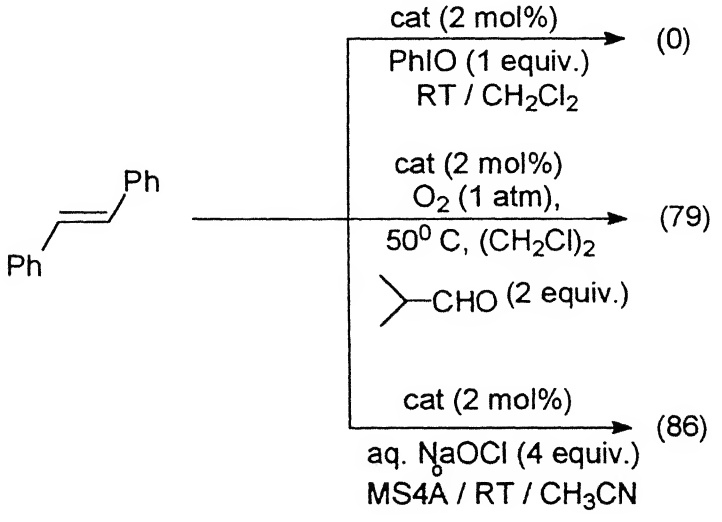
Use of n-butanal as reductant resulted in the formation of epoxide in very low yield, but the use of aldehydes having secondary or tertiary carbon next to the carbonyl carbon, such as 2-methylpropanal, cyclohexanecarboxaldehyde etc., yielded epoxide in quantitative yields.

Katsuki and coworkers[55] have described monooxygenation of alkenes by using nickel catalyst, [N,N^1-bis[O-(P-toluenesulfonylamino) benzylidene]ethylenediaminato] nickel(II), in the presence of 2-methylpropanal (Scheme 26).



Scheme 26

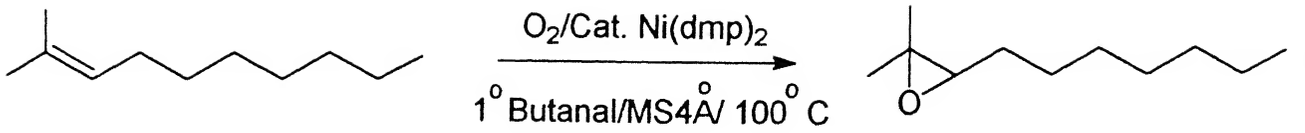
Contrary to the (salen) manganese(III) complexes, no epoxidation was observed when iodosylbenzene was used as terminal oxidant. However, dioxygen in the presence of aldehyde was found to be an effective oxidant and the reaction proceeded smoothly at 50°C to give the corresponding epoxide in good yield. Epoxidation with aqueous sodium hypochlorite in the presence of molecular sieves 4A also afforded the epoxide in good yield but substrates other than trans-stilbene were poorly epoxidised under these conditions (Scheme 27)[55].



Scheme 27

The reducing ability of aliphatic and aromatic aldehydes was measured using clayniac as catalyst in the presence of cyclohexene and molecular oxygen. Isobutanal was confirmed as the best sacrificial auxiliary. Observed inhibitions by p-benzoquinone and by TEMPO clearly point out the radical nature of this reaction[56].

Mukàiyama and coworkers have described epoxidation of alkenes using $Ni(dmp)_2$ [(bis(1,3-di(p-methoxyphenyl)-1,3-propane-dionato) Nickel(II)] as catalyst in the presence of alcohol and dioxygen (Eq. 11). In this reaction, primary alcohol acts as a good reducing agent. Aromatic alkenes substituted with electron withdrawing groups were epoxidised in high yields (Table 7)[57].



96 97 Eq. 11

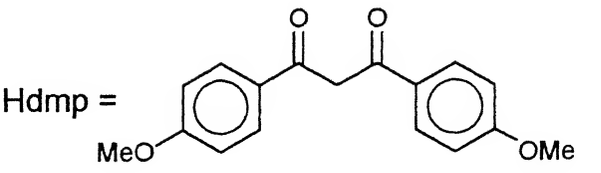
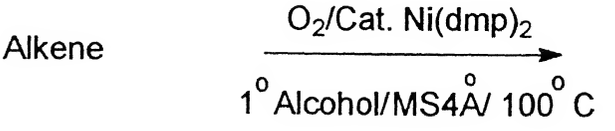
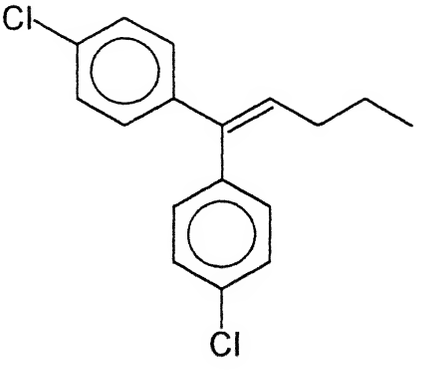
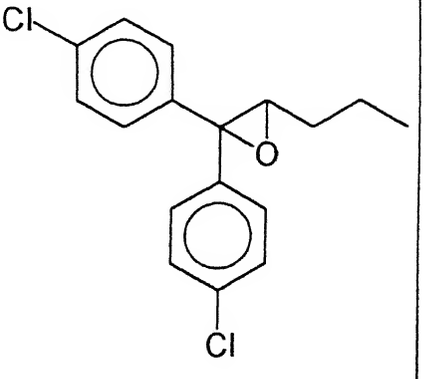
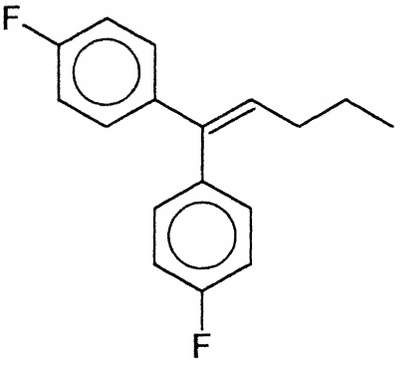
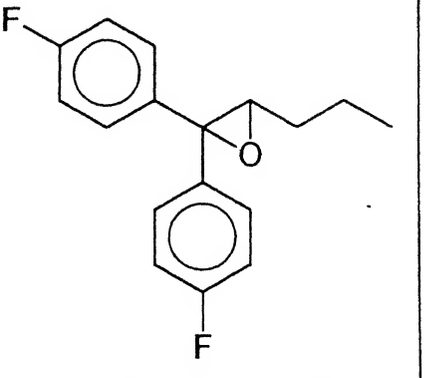


Table 7. Epoxidation of Various Alkenes Catalysed by Ni(dmp)$_2$



Entry	Alkene	Alcohol	Time / h	Epoxide
1		n- $C_{14}H_{29}OH$	8	
2		n- $C_{14}H_{29}OH$	4	

Bouhlel and coworkers[58] have carried out the epoxidation of alkenes using clay-impregnated nickel catalyst in the presence of isobutanal and dioxygen. This reaction was performed at room temperature by compressed air to afford the epoxide in moderate yields.

The generation of acyl radicals by a catalytic route is a challenging task as methods described above involve stoichiometric amounts of acyl radical precursor(eg. selenoesters, xanthates and acyl cobalt). Secondly, in the case of tributyltin mediated radical reactions the product radical center is terminated by hydrogen atom transfer without functionality which limits the scope of these methodologies.

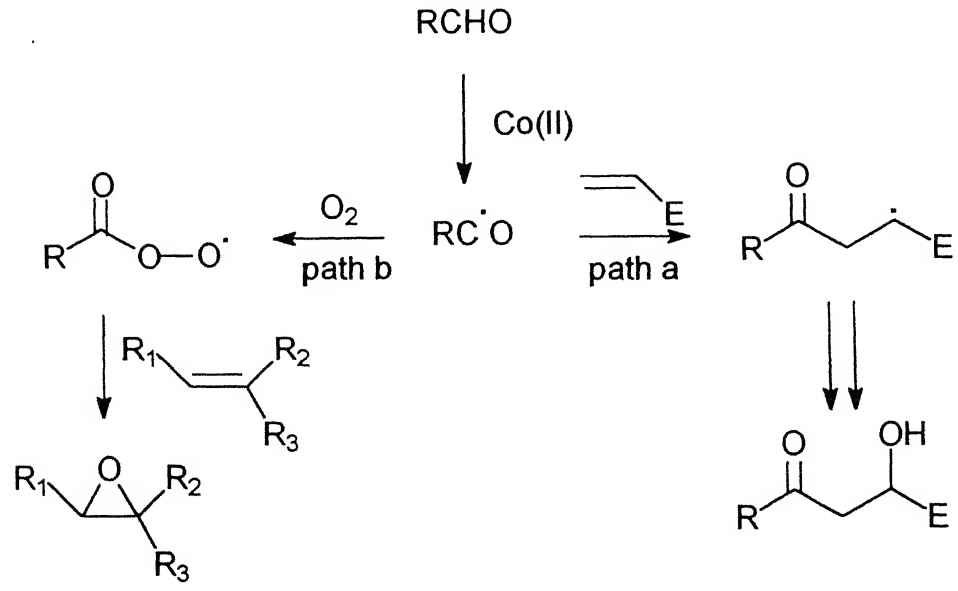
Epoxides are highly useful synthetic intermediates, although number of methods are known for the synthesis of this class of compounds, efficient , mild and inexpensive methods are very limited.

In view of the above limitations, we have explored the possibility of generating the acyl radicals in catalytic manner under extremely mild conditions. The following section deals with generation of acyl radical and subsequent reactions, such as oxidative addition with activated alkenes, epoxidation of unactivated alkenes by cobalt(II) Schiff base complexes as catalyst in the presence of dioxygen and coreducing agent (aldehydes).

1.2 Present Study

We have observed that the acyl radical can be generated from enolizable aldehydes in the presence of cobalt(II) Schiff base complexes. Subsequently, these radicals can be trapped

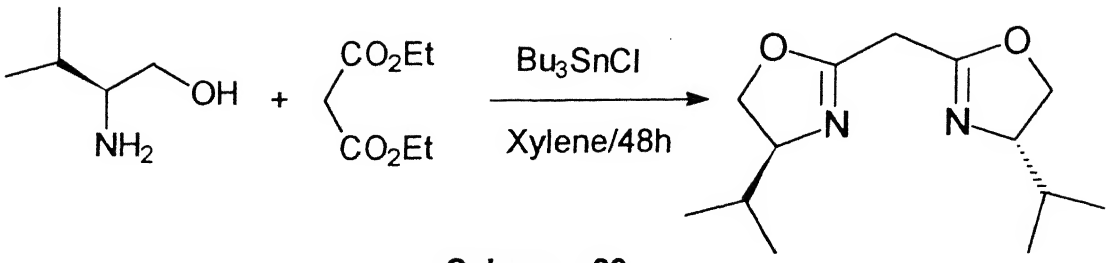
with electron deficient alkenes and the resulting product radical is terminated by incorporation of dioxygen to give 2-hydroxy-4-oxoester or nitrile (path a, Scheme 28). On the otherhand, the formation of epoxides which are presumably derived as a result of oxygen capture by the acyl radical (path b, Scheme 28). We report here the results of our findings.



Scheme 28

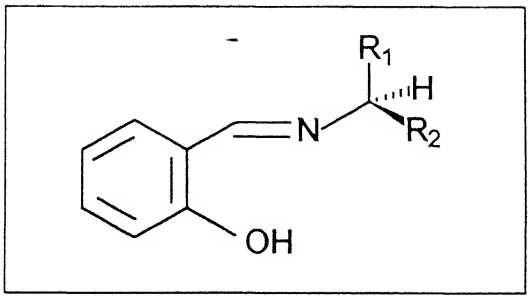
1.2.1 Preparation of Schiff Base Ligands

A series of Schiff base ligands **98a-g** were prepared by reacting aromatic aldehyde with chiral amine (Table 8). Thus, the reaction between salicylaldehyde and (S)-(-)-α-methylbenzyl-amine resulted in the formation of the corresponding Schiff base ligand **98a** in quantitative yield. In the same way, the Schiff bases ligands **98b-e** were derived from salicylaldehyde and methyl ester of amino acids. The reaction between (L)-histidine methyl ester and acetylacetone afforded the ligand **98g** in good yield. The ligand, bisoxazoline[59], **98f** was prepared by the reaction of 2-amino-3-methyl-1-butanol and diethyl malonate (Scheme 29).

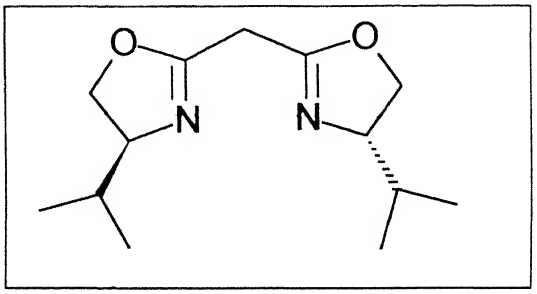


Scheme 29

Table 8. Schiff Base Ligands Derived from α–(L)-Amino Acids Ester, Amine, Alcohols and Aromatic Aldehydes

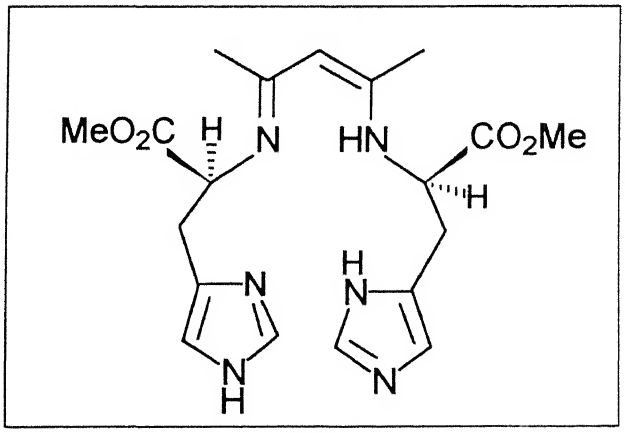


98



98f

Ligand	R_1	R_2
98a	CH_3	Ph
98b	CH_2Ph	CO_2Me
98c	CH_2OH	CO_2Me
98d	$CHCH_3OH$	CO_2Me
98e	CH_2CH_2SMe	CO_2Me



98g

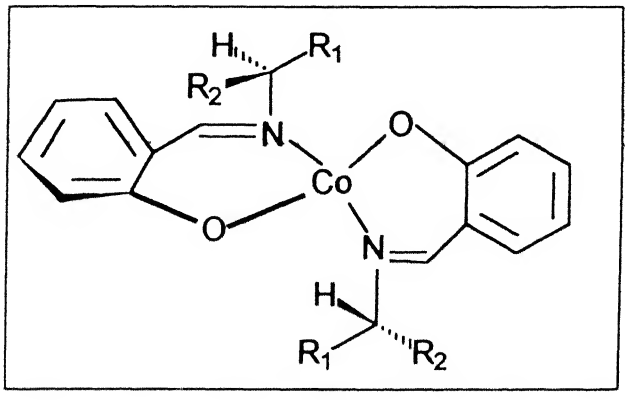
1.2.2. Preparation of Cobalt(II) Schiff Base Complexes

A variety of cobalt(II) complexes **99a-g** have been prepared by reacting preheated (110° C) cobalt(II) chloride and the Schiff base ligands **98a-g** described in table 8. The reaction was performed under nitrogen atmosphere by mixing the stoichiometric amount of cobalt(II) chloride and ligand at ambient temperature. The chiral complexes were isolated as powder on crystallization. They were characterized by the physical techniques such as UV-VIS, magnetic moment, EPR, conductivity and FAB mass analysis. Most of these complexes are stable in air and are soluble in acetonitrile and exhibit green color (Table 9).

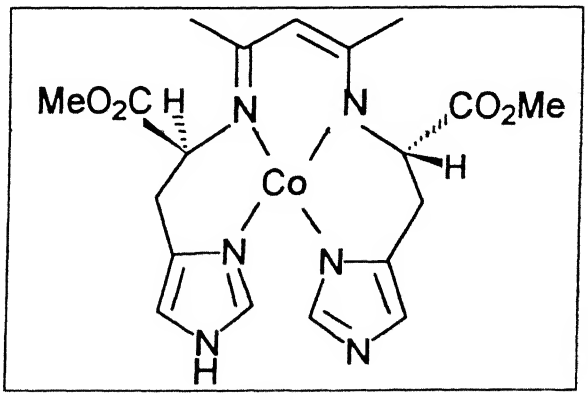
Table 9. Cobalt(II) Complexes Derived from Chiral Schiff Base Ligands Under Nitrogen

$$CoCl_2 + mLn \xrightarrow{N_2} Co(Ln)_m$$

m=1,2 ; m=1,2 ; Ln=Schiff Base Ligand

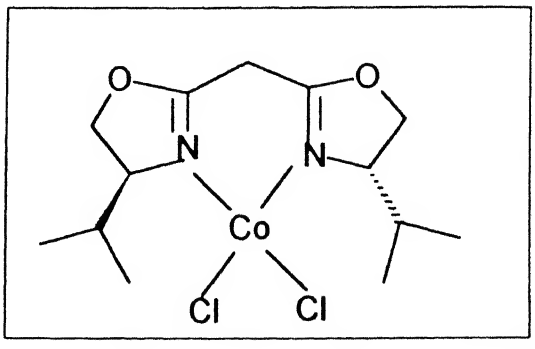


99



99g

Catalsyt	R_1	R_2
99a	CH_3	Ph
99b	CH_2Ph	CO_2Me
99c	CH_2OH	CO_2Me
99d	$CHCH_3OH$	CO_2Me
99e	CH_2CH_2SMe	CO_2Me



99f

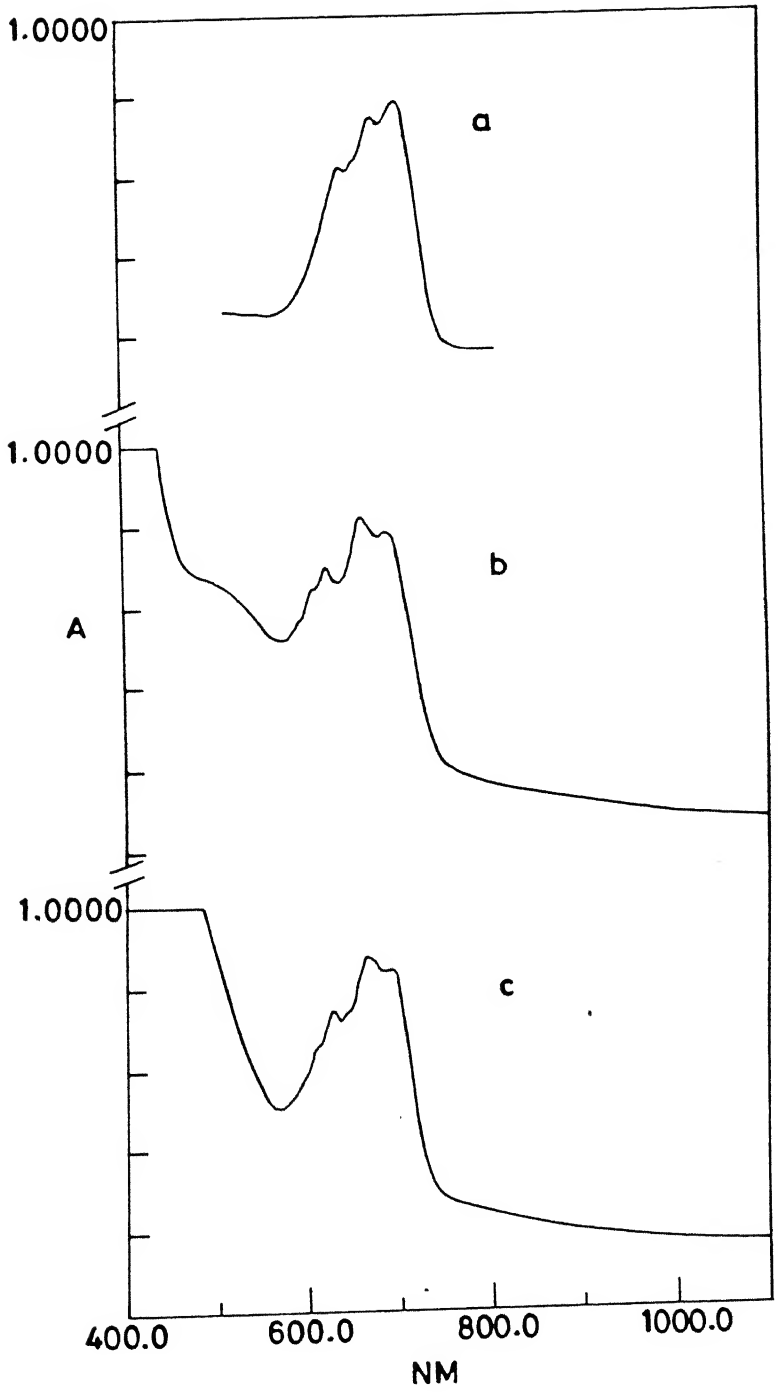


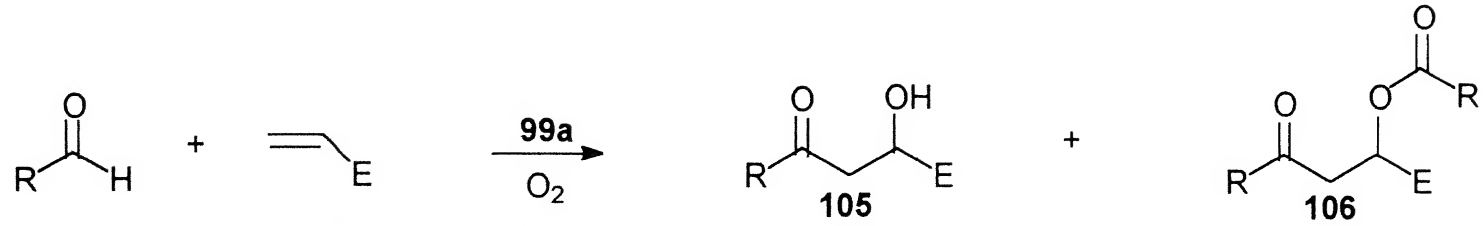
Fig2. UV-Vis spectra : a. Complex **99a** ; b. Complex **99b** ; c. Complex **99c**.

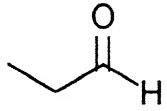
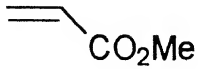
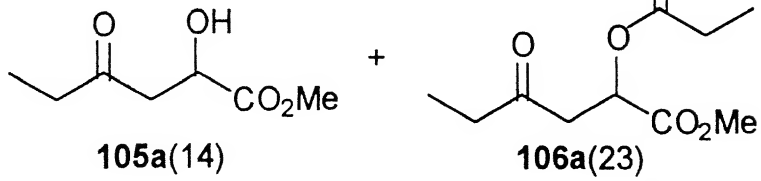
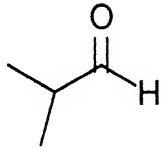
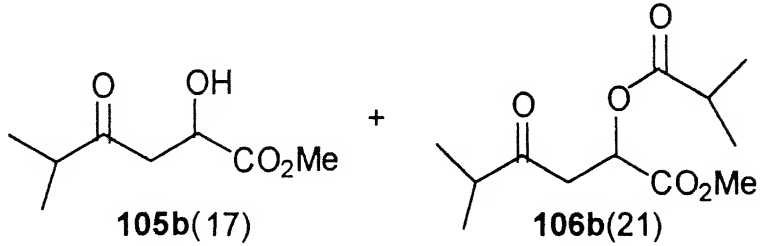
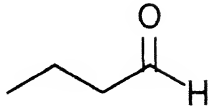
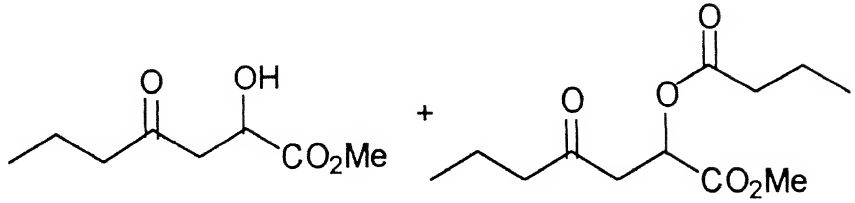
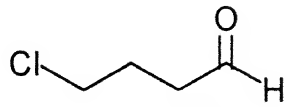
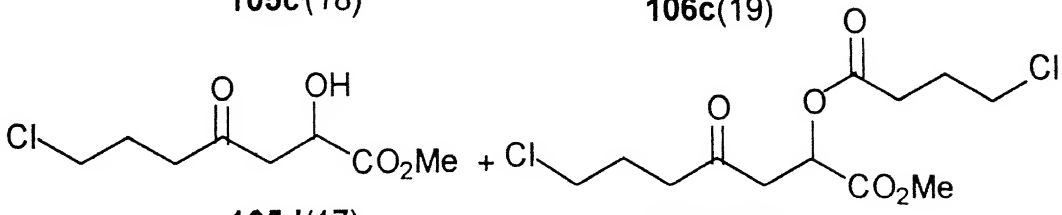
1.2.3 Reaction with Electron Deficient Alkenes

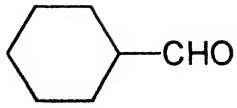
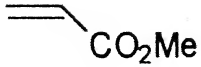
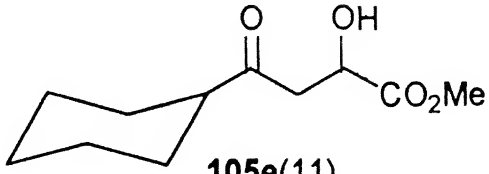
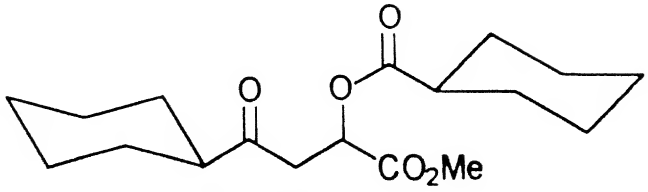
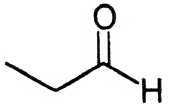
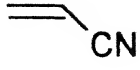
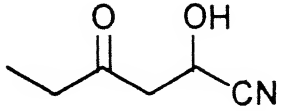
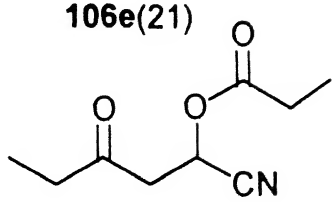
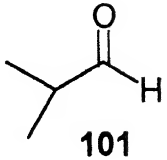
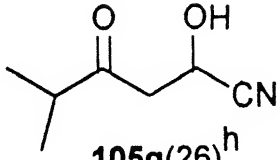
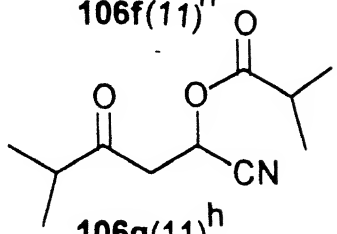
The cobalt(II) catalyzed reaction of activated alkenes with aldehydes and dioxygen afforded a mixture of 2-hydroxy and 2-acyloxy-4-oxoesters or nitriles **105-106** in good yields (Table 10, entries 1-7). The catalyst **99a** is quite efficient in effecting this transformation as the ratio of 2-hydroxy and 2-acyloxy-4-oxoesters varied when these reactions were conducted with different catalysts. Polymerization was found to be the major pathway if the reactions were carried out under nitrogen atmosphere. These reactions are always accompanied by 40-50% of the carboxylic acid and anhydride derived from the corresponding aldehydes, however, an exact quantification of the product was obscured by its loss during the workup. Careful analysis of the reaction mixture revealed the absence of any unchanged aldehyde, however, some unreacted methyl acrylate or acrylonitrile was observed. The mass balance of these reactions clearly reveal that approximately 40% of the aldehyde is converted into the addition products and the remaining aldehyde is transformed to a mixture of the corresponding carboxylic acid and anhydride.

The reaction of propanal with methyl acrylate was carried out using different cobalt(II) catalysts **99a, 99e** and **99g** in the presence of dioxygen (Table 11, Entries 1-3). It is interesting to note that the ratio of 2-hydroxy and 2-acyloxy-4-oxoesters **105** and **106** were remain unaffected in the case of **99a** and **99e** whereas catalyst **99g** gave only the acyloxy compound **106a** as the product. It is clearly evident that the outcome of these reactions are controlled by the nature of ligand around the metal center.

Table 10. Cobalt(II) Catalysed Reaction of Aldehydes with Electron Deficient Alkenes and Dioxygen

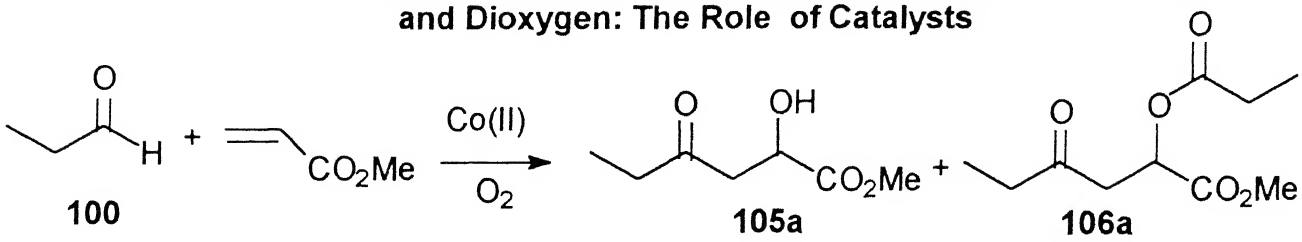


Entry	Aldehyde	Alkene	Product(% Yield)
1	 **100**		 **105a**(14) + **106a**(23)
2	 **101**		 **105b**(17) + **106b**(21)
3	 **102**		 **105c**(18) + **106c**(19)
4	 **103**		 **105d**(17) + **106d**(24)

5	 **104**		 **105e**(11)	+	 **106e**(21)
6	 **100**		 **105f**(25)[h]	+	 **106f**(11)[h]
7	 **101**		 **105g**(26)[h]	+	 **106g**(11)[h]

[h] *$CoCl_2$ was used as catalyst.*

Table 11. Cobalt(II) Catalysed Reaction of Aldehydes with Electron Deficient Alkenes and Dioxygen: The Role of Catalysts



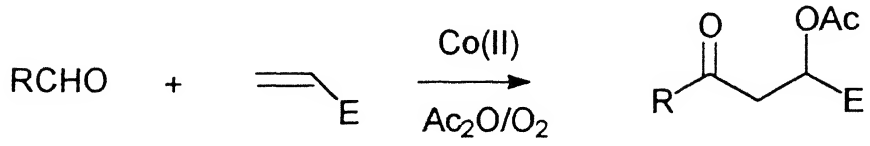
100 **105a** **106a**

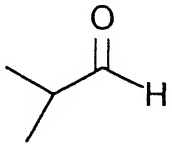
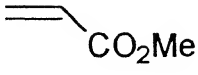
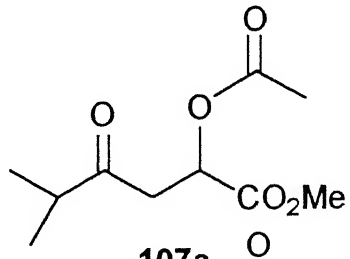
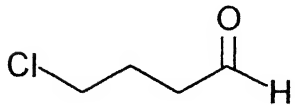
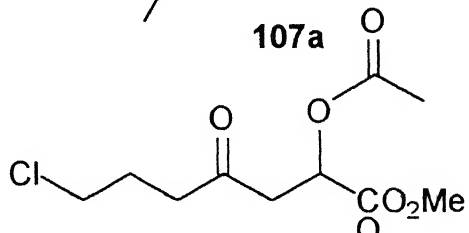
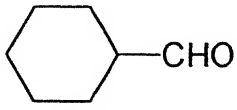
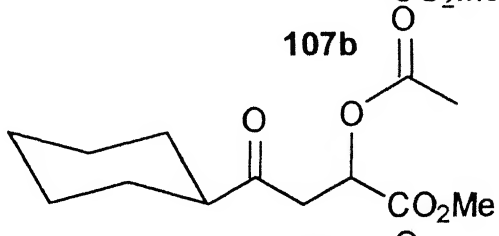
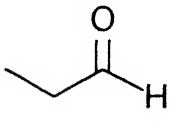
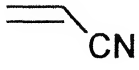
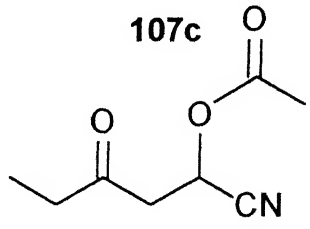
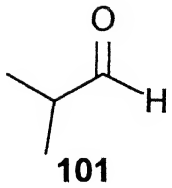
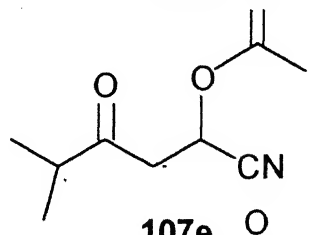
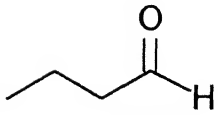
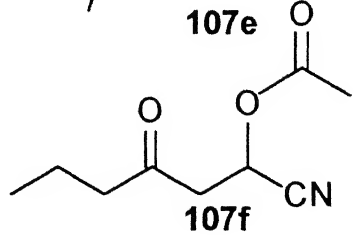
Entry	Catalyst	Product(% Yield)	
1	**99a**	14	23
2	**99e**	13	19
3	**99g**	-	31

The addition of aldehyde to methyl acrylate or acrylonitrile is successful only if excess of the latter is used. However, no adduct was formed if the aldehydes and activated alkenes were used in stoichiometric amounts. Aldehydes mainly gave the corresponding carboxylic acid and anhydride under these conditions and no attempt was made to optimize the formation of these products. The 2-acyloxy compounds **106a-g** may be resulting due to the acylation of the hydroxy compounds **105a-g** by the anhydrides derived from the corresponding aldehydes.

Interestingly, in the presence of excess (3 equivalent) of acetic anhydride the corresponding 2-acetoxy compounds **107a-f** were obtained in high yields(Table 12, Entries 1-6). It is noteworthy that no 2-acyloxy compounds were obtained under these conditions. Cobalt(II) chloride was found to be the most suitable catalyst for these transformations, however, the Schiff base complexes were able to affect this transmutation only in modest yields. The formation of 2-hydroxy compounds was suppressed considerably in the presence of acetic anhydride. Also, no significant quantity of the carboxylic acid derived from the corresponding aldehyde was observed in these reactions with acetic anhydride. Acetic acid and unchanged acetic anhydride was also obtained in this reaction, however, no quantification of the products could be done as significant loss of these were observed during the work up process.

Table 12. Cobalt(II) Catalysed Reaction of Aldehydes with Electron Deficient Alkenes in the Presence of Acetic Anhydride and Dioxygen



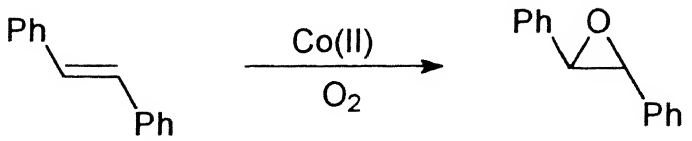
Entry	Aldehyde	Alkene	Product	Yield%
1	 **101**		 **107a**	77
2	 **103**		 **107b**	56
3	 **104**		 **107c**	55
4	 **100**		 **107d**	58
5	 **101**		 **107e**	56
6	 **102**		 **107f**	53

1.2.4 Reaction with Unactivated Alkenes

Cobalt(II) catalyzed reaction of unactivated alkenes with aldehydes and dioxygen resulted into the formation of the corresponding epoxides (Table 14). Thus, (E)-stilbene can be converted to trans-epoxide **120** with various aldehydes (Table 13). Best results are obtained when 2-methylpropanal **101** was used as coreducing agent, however, n-propanal **100**, cyclohexanecarboxaldehyde **104** and citronellal **110** afford in moderate to good yields of the epoxide. Reaction with aromatic aldehydes, benzaldehyde and 4-methoxybenzaldehyde, remain unaffected, however, the latter were transformed to the corresponding acids. The epoxidation of (E)-stilbene using citronellal results into the formation of the lactone **144** besides trans stilbene oxide (Table 13, Entry 7). The lactone may be derived from citronellal via an epoxidation of the double bond followed by intramolecular cyclization.

A series of alkenes were epoxidised using 2-methylpropanal **101** and **99c** in the presence of dioxygen (Table 14). All the catalysts **99a-g** mentioned in table 9 are efficient in effecting this transformation and the results using **99c** are presented in table 14. 1-Dodecene is epoxidised in high yield without any observable addition product. The geometrically pure alkenes ie., (E)-stilbene **108** and (Z)-2-octene **113** were smoothly transformed to the corresponding epoxides along with trace amount of the regioisomeric epoxides (Table 14, Entries 2-3). 1,7-Octadiene was monoepoxidised in moderate yields whereas dienes **115-116** with electronically dissimilar double bonds were chemoselectively epoxidised to the corresponding monoepoxide (Table 14, Entries 5-6). It is noteworthy that in these cases no regioisomeric epoxides were observed which is in contrast to the similar epoxidation using nickel (II) complexes. The monoepoxidation of the triene **118** clearly indicates that these epoxidations are quite facile in the case of highly substituted double bonds (Table 14, Entry 8).

Table 13 : Cobalt(II) Catalyzed Reaction of Aldehydes with (E)-Stilbene in the Presence of Dioxygen



108 **120**

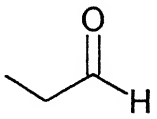
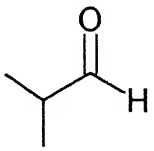
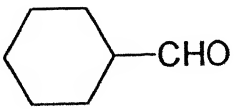
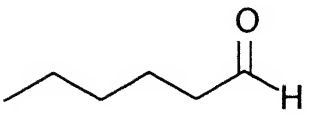
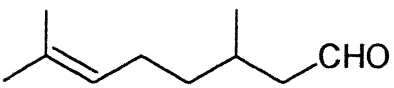
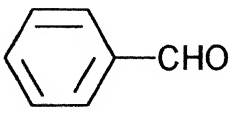
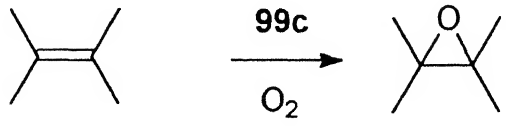
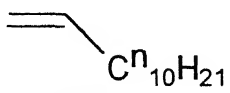
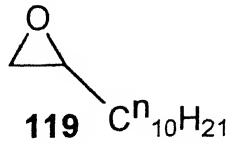
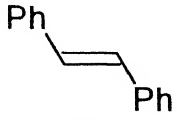
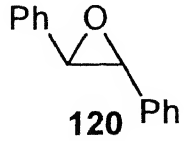
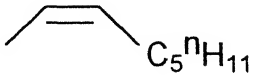
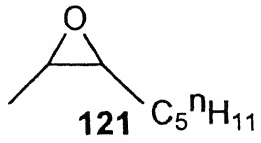
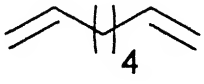
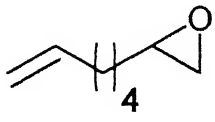
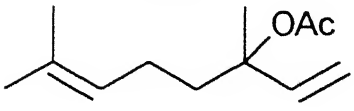
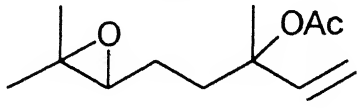
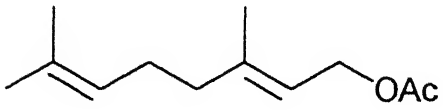
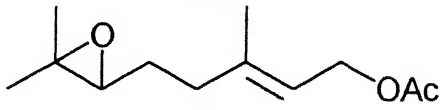
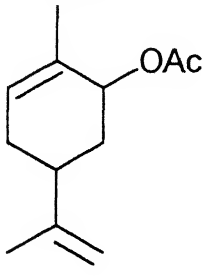
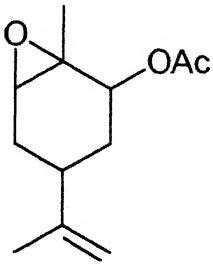
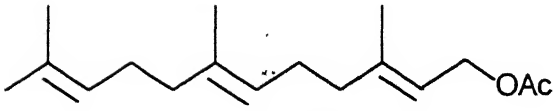
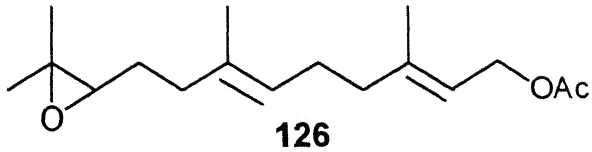
Entry	Aldehyde	Catalyst	Product(% yield)
1		**99c**	52
2		**99c**	77
3		**99b**	89
4		**99g**	72
5	 **104**	**99c**	59
6	 **109**	**99c**	65
7	 **110**	**99g**	68
8	 **111**	**99f**	-

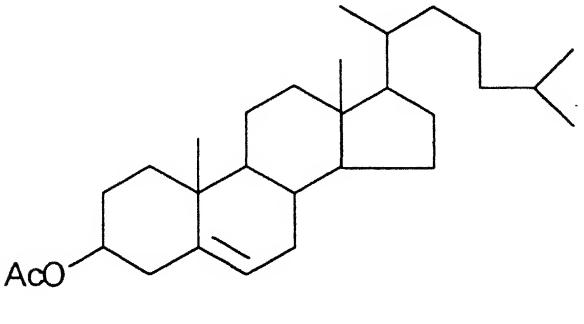
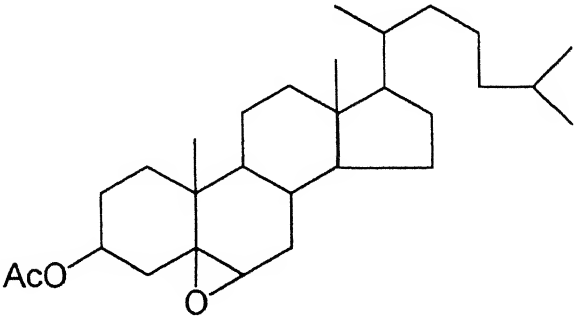
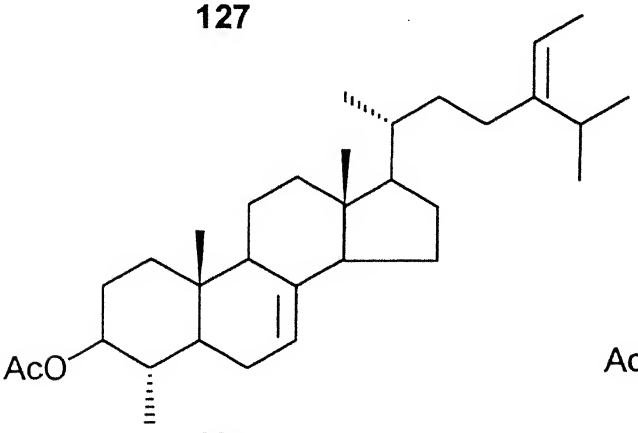
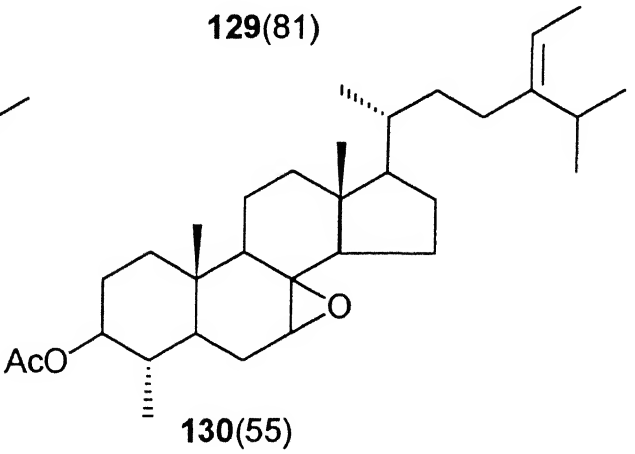
Table 14. Cobalt(II) Catalysed Epoxidation of Various Alkenes with Dioxygen and 2-Methyl propanal



Entry	Alkene	Product	% Yield
1	 **112**	 **119**	55
2	 **108**	 **120**	77
3	 **113**	 **121**	39
4	 **114**	 **122**	44
5	 **115**	 **123**	70
6	 **116**	 **124**	66
7	 **117**	 **125**	52
8	 **118**	 **126**	45

The epoxidation of cholesteryl acetate **127** and α_1-sitosterol acetate **128** were carried out using catalyst **99c** in the presence of 2-methylpropanal and dioxygen, it is noteworthy that the major product was found to be α-epoxides (Table 15). It is interesting to note that in the case of α_1-sitosterol acetate, the cyclic double bond underwent epoxidation selectively whereas the side chain trisubstituted double bond was intact.

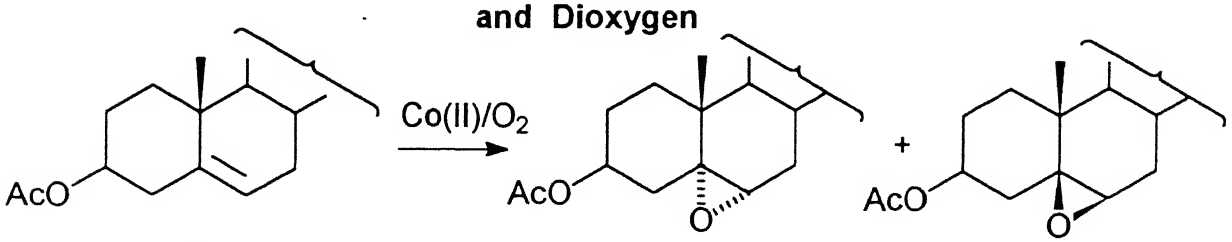
Table 15. Cobalt(II) Catalysed Epoxidation of Alkenes In the Presence of Dioxygen

Entry	Alkene	Product(% Yield)
1	 **127**	 **129**(81)
2	 **128**	 **130**(55)

The epoxidation of cholesteryl acetate **127** was examined in the presence of different catalysts **99c, 99f** and **99g** under these conditions. All the catalysts gave α-epoxide as the major product which is similar to the reaction of m-chloroperbenzoic acid[60] (Table 16). This observation clearly suggests that cobalt(II) catalyzed epoxidation are mechanistically quite

different from the corresponding nickel(II) promoted epoxidations[54,55].

Table 16. Cobalt(II) Catalysed Epoxidation of Cholesterylacetate with 2-Methylpropanal and Dioxygen



127 **129a** **129b**

Entry	Catalyst	Yield % α-epoxide:β-epoxide
1	**99c**	81 (75:25)
2	**99f**	72 (72:28)
3	**99g**	87 (80:20)

Cyclic alkenes behaved quite differently under these reaction conditions as no epoxide formation was observed. Thus, cyclohexene provided a mixture of three products on treatment with isobutanal and dioxygen in the presence of catalyst **99c** (Table 17). A careful analysis of this mixture indicated that 2-cyclohexen-1-ol and 2-cyclohexen-1-one were obtained as 1:2 mixture whereas cyclohexene oxide was present in minor amounts. Surprisingly, cycloalkenes larger than cyclohexene functioned quite differently and they were transformed to the corresponding ketones in very high yields. Thus, cycloheptene, cyclooctene and cyclododecene were converted to their corresponding ketones in very good yields. Surprisingly, cycloheptene also affords the corresponding enone in moderate yield. Interestingly, the reaction of (+)-longifolene under these conditions gave the corresponding carboxylic acid as the major product.

Table 17. Cobalt(II) Catalysed Oxidation of Alkenes in the Presence of Dioxygen and 2-Methyl Propanal

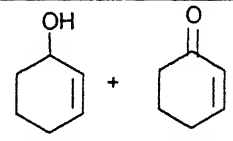
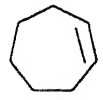
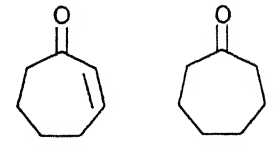
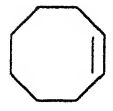
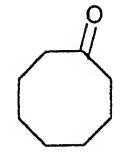
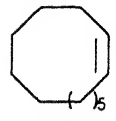
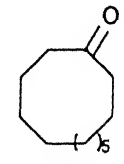
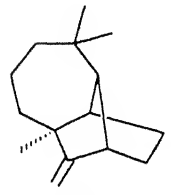
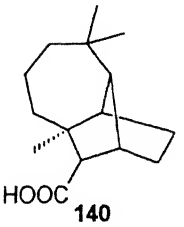
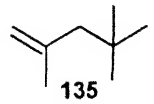
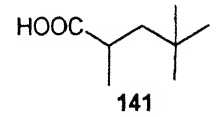
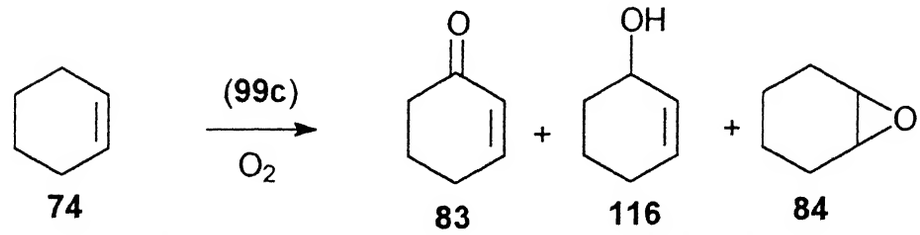
Entry	Alkene	Catalyst	Product	% Yield
1	 **74**	**99c**	 **116** + **84**	72(1:2)
2		**99f**		61(1:3)
3	 **131**	**99c**	 **136** **137**	67(1:3)
4		**99f**		52(2:3)
5	 **132**	**99c**	 **138**	65
		99f		40
6				
7	 **133**	**99c**	 **139**	62
8	 **134**	**99c**	 HOOC **140**	65
9	 **135**	**99c**	 HOOC **141**	59

Table 18. Cobalt(II) Catalysed Allylic Oxidation of Cyclohexene: The Effect of Aliphatic Aldehydes



74 **83** **116** **84**

Entry	Aldehyde	Products(% Yield)[a]
1	**100**	55(2:1:0.5)
2	**101**	72 (2:1:0)
3	**104**	33(1.5:1:0)
4	 **142**	32(1.6:1:0)

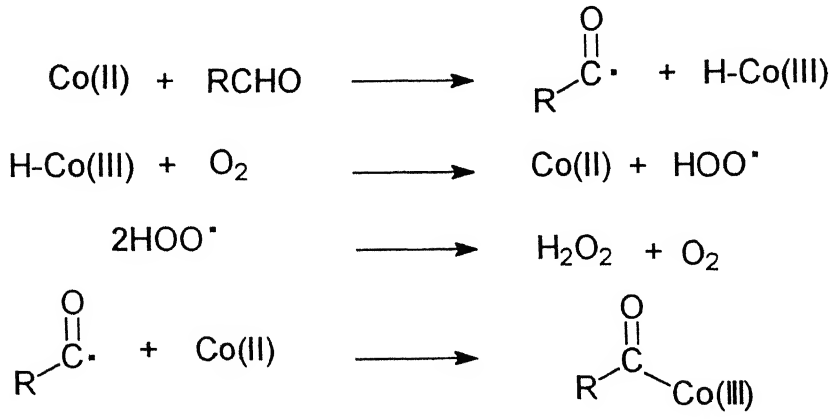
[a] *Ratio was determined by Gas Chromatography.*

The reaction of cyclohexene with different aldehydes was examined using catalyst **99c** in the presence of dioxygen. Once again, the branched aldehyde 2-methylpropanal was found to be suitable in effecting this transformation to give the corresponding enol and enone in the ratio of 1:2 in high yield whereas hexanal gave in moderate yield. Surprisingly, propanal provided cyclohexene oxide as minor product in addition to the enone and enol (Table 18).

The formation of ketones from cyclic alkenes may be proceeding via the rearrangement of initially formed epoxide. Thus, the conversion of (+)-longifolene to the corresponding carboxylic acid may be explained first by formation of epoxide which will undergo rearrangement to the corresponding aldehyde. The latter will undergo oxidation to the corresponding carboxylic acid under the reaction conditions. We have already shown aldehydes can be oxidised to the corresponding carboxylic acid by cobalt(II) complex and dioxygen.

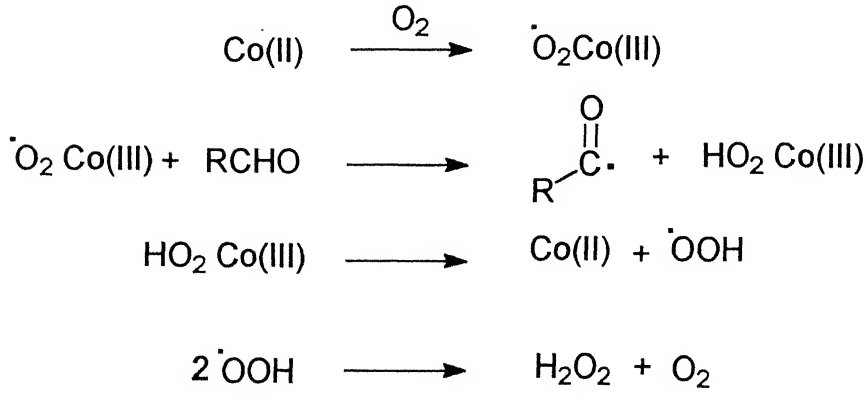
1.2.5 Mechanism

The dichotomous nature of these reactions suggests that a common intermediate may be involved whose reactivity is dependent upon the nature of the alkene. The catalytic redox reaction of aldehyde with cobalt(II) to give a hydrido cobalt species and an acyl radical (Scheme 30). Mimoun has proposed a hydridocobalt species from the reaction of CoSMPDT



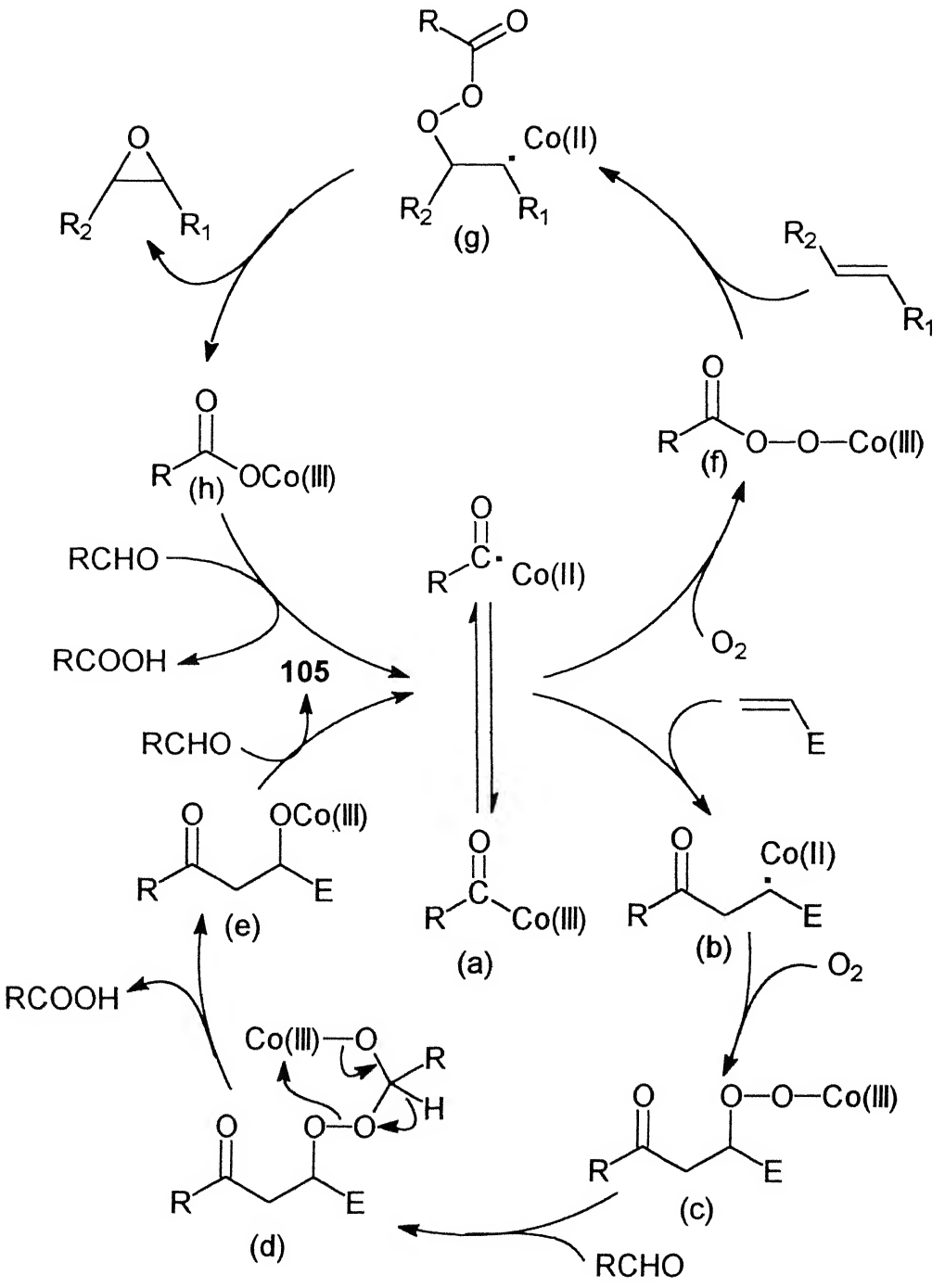
Scheme 30

with alcohol. The reaction of dioxygen with hydrido species may regenerate the catalyst **99** and hydroperoxy radical, which is likely to fragment at a diffusion controlled rate to hydrogen peroxide and dioxygen (Scheme 31). The acyl radical may exist as an acyl-cobalt(III) complex;



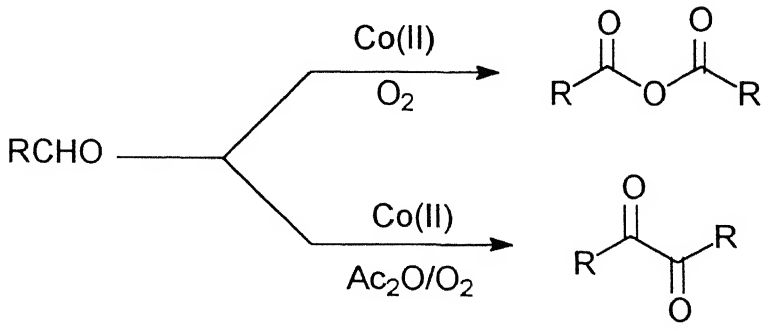
Scheme 31

however, in the presence of oxygen it may just be a transient species. Alternatively, acyl radical formation can also be initiated by interaction of an oxygen of **99** with aldehyde, and the hydroperoxy cobalt complex[61] thus formed may spontaneously disproportionate to hydrogen peroxide and oxygen (Scheme 32). The acyl radical may then interact with cobalt complex to provide (a) acylcobalt(III) species. The acyl radical will react with electron deficient alkene to give an adduct radical (b) which may readily undergo insertion[62] of dioxygen to yield a peroxycobalt intermediate (c) (Scheme 32). The reaction of (c) with aldehyde may provide a labile intermediate (d) which will fragment readily to afford the alkoxy cobalt complex (e) and the corresponding carboxylic acid. A redox reaction between another molecule of aldehyde and the complex (e) may provide the 2-hydroxy-4-oxoesters or nitriles **105**, and the acyl radical or acyl cobalt complex (a) will be regenerated to complete the cycle. The acyl radical generated from acyl cobalt complex is known to undergo 1,4-addition to electron deficient alkenes under thermal or photochemical conditions. The cobalt carbon bond may not survive in the presence of dioxygen, and therefore, the adduct (b) is likely to be free radical. However, the reduction of the peroxy species (c) with aldehydes via the intermediate (d) will probably be mediated by the cobalt complex as the fragmentation of (d) to give (e) and carboxylic acid may not be favored by a free radical process. Alternatively, in the presence of unactivated alkenes the acyl radical or acyl cobalt complex (a) will undergo the insertion of dioxygen, instead of addition to the alkene, to yield peroxycobalt species (f) which may react with the alkene (Scheme 32) to give a peroxyacyl organocobalt intermediate (g). A homolytic fragmentation of the latter will afford the corresponding epoxide and the cobalt carboxylate (h), and the latter may interact with aldehyde via a redox process to generate the acyl radical or acylcobalt complex (a). The cobalt(II) catalyzed epoxidation of the alkenes with dioxygen is also known to occur via a β-peroxy radical which resembles the proposed intermediate (g). The nonobservance of epoxide


R
O
O
O
Co(II)
R2
R1
(g)
O
R2
R1
R2
R1
O
R
O—O—Co(III)
(f)
O
R
OCo(III)
(h)
RCHO
RCOOH
105
RCHO
O
R
Co(II)
O2
E
O
R
OCo(III)
E
(e)
O
R
C
Co(III)
(a)
O
R
Co(II)
E
(b)
O2
RCOOH
Co(III)—O
R
H
O
O—O
R
E
(d)
O
O—O—Co(III)
R
E
(c)
RCHO

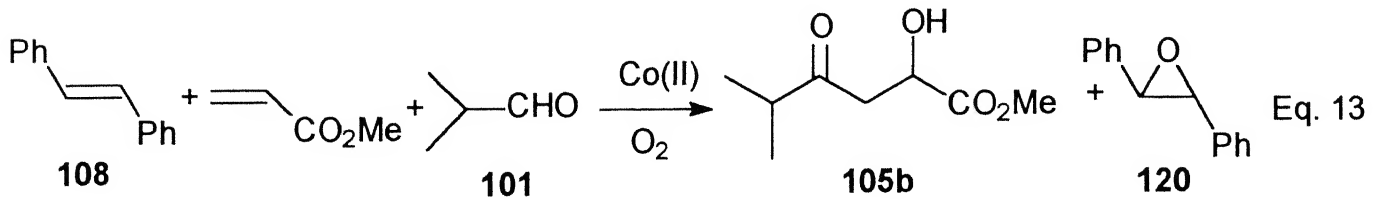
Scheme 32

in the presence of acetic anhydride is not surprising, as our earlier studies have shown that its presence favor the formation of 1,2-diones from aldehydes, whereas its absence leads to the corresponding carboxylic acid and anhydride . This implies that the acyl radical is not very efficient in capturing the dioxygen in the presence of excess of acetic anhydride, thus, the addition of this radical to an electron deficient alkene or its self coupling become favored pathways (Scheme 33).



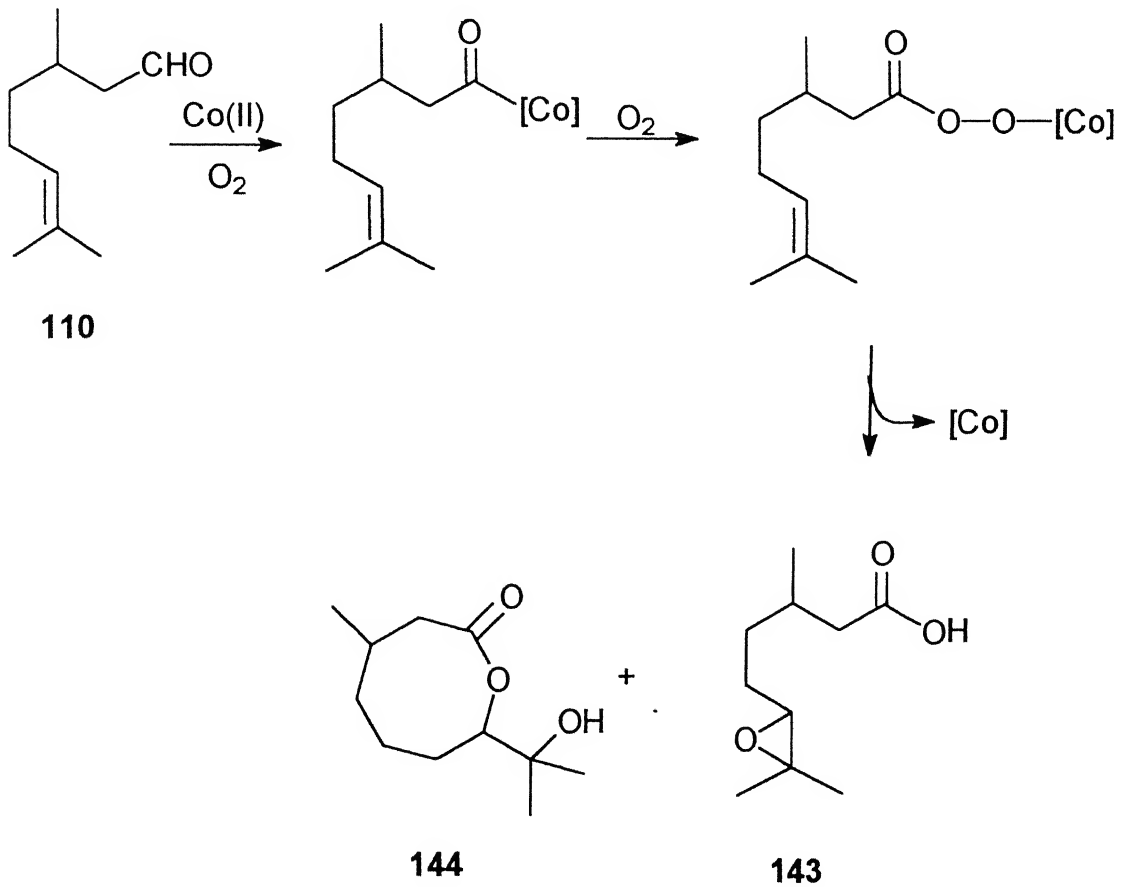
Scheme 33

Finally, the presence of a common intermediate (a) is demonstrated by performing the reaction in the presence of a mixture of the electronically dissimilar alkenes. Thus, 2-methylpropanal **101** reacted with both stilbene and excess of methyl acrylate to afford a mixture of the corresponding epoxide and 2-hydroxy-4-oxoester in good yields (Eq. 13).



108 **101** **105b** **120** Eq. 13

In order to further demonstrate the intermediacy of a acylcobalt intermediate, we undertook a study on the reaction of citronellal **110** which gave a mixture of compounds from which two compounds were isolated in moderate yields (Scheme 34). The formation of the epoxy acid and the lactone **144** clearly indicate that the products are obtained by intramolecular epoxidation which occur as a consequence to the incorporation of dioxygen in the initially formed acyl cobalt complex from citronellal. The initially formed epoxy acid undergoes intramolecular lactonization to yield **144**. The above reaction clearly supports that these transformations are proceeding via a common intermediate whose reactivity depends on the nature of the alkene.



110 **144** **143**

Scheme 34

Finally, in order to prove the changes in the oxidation state of cobalt complex, as described in catalytic cycle (Scheme 32), the reaction was examined by UV-VIS studies. Thus, the reaction between propanal and methyl acrylate was monitored periodically with UV-VIS spectrophotometer and the spectra recorded at different time interval are presented in fig.2. It is quite clear that the cobalt(II) complex (Spectrum a, Fig. 2) disappears after 15h (Spectrum b, Fig.2) and as soon as reaction goes to completion it reappears (Spectrum c, Fig.2). The UV-VIS monitoring of the reaction strongly supports the catalytic cycle proposed in Scheme 32.

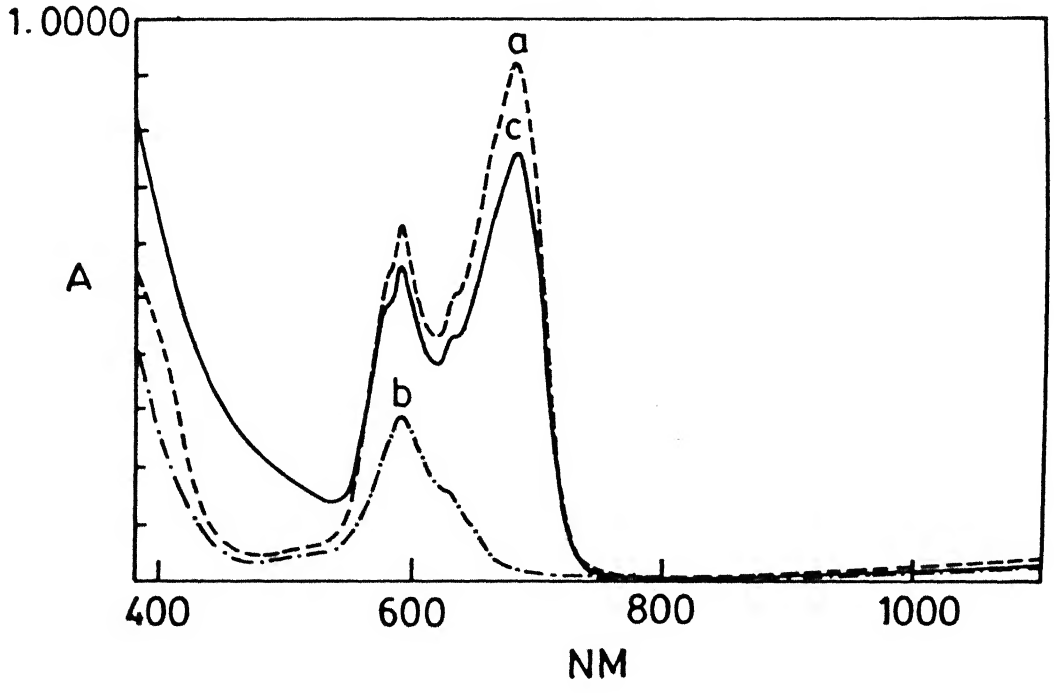


*Fig. 2 . Vis spectra of the reaction propanal **100** with methylacrylate and catalyst **99a:** (a) spectrum at the beginning of the reaction. (b) Spectrum of the reaction mixture after 15h. (c) Spectrum of the isolated catalyst after the completion of the reaction.*

Cobalt(II) Catalyzed Oxidation of Secondary Alcohols with Dioxygen in the Presence of 2-Methylpropnal

2.1 Introduction

Metal catalyzed oxidation of alcohols to carbonyl compounds in the presence of dioxygen constitutes[28] one of the most important and desirable chemical transformation. Considerations based on environmental pollution have imposed severe restrictions mainly to develop cleaner technologies with negligible inorganic salt formations and in view of these considerations, catalyst with optimal atom utilization seems to be an attractive proposition in achieving the above transformation. As a result of this, the oxidation of organic substrate by molecular oxygen in the presence of metal catalyst provides the most formidable alternative to the existing mode of oxidations. Oxidation of alcohols to carbonyl compounds can be catalyzed with transition metals in the presence of various oxygen atom donors. The following section deals with the review of the reaction catalyzed by various metal complexes.

Martin and coworkers[63] have reported that rhodium trichloride acts as a very effective catalyst for the selective oxidation of secondary alcohol to carbonyl compounds in the presence of bismuth trichloride, lithium chloride and molecular oxygen (Eq. 14).

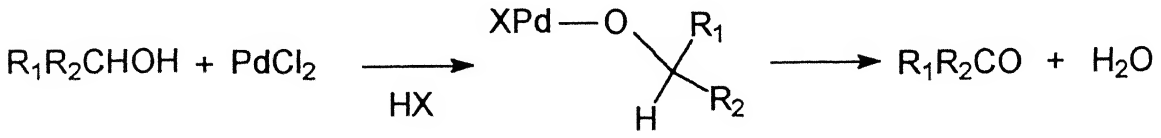
$$2\ R_1R_2CHOH + O_2 \xrightarrow{RhCl_3/BiCl_3/LiCl} 2R_1R_2CO + 2H_2O \qquad \text{Eq. 14}$$

Palladium Salt

Palladium compounds are effective catalysts for the selective oxidative transformation of primary and secondary alcohols into carbonyl compounds. Although conventional $PdCl_2/CuCl_2$ catalysts can be operated at 70-120° C and under molecular oxygen pressure (3 atm)[64], milder procedures using $PdCl_2$/NaOAc mixture are effective at room temperature and atmospheric oxygen pressure (Eq. 15).

$$R_1R_2CHOH + 0.5O_2 \xrightarrow[38^oC]{PdCl_2/NaOAc} R_1R_2CO + H_2O \qquad \text{Eq. 15}$$

The mechanism of this transformation presumably involves palladium alkoxide formation followed by β-hydride elimination (Scheme 35)[65].

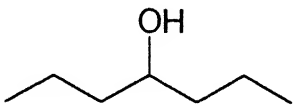
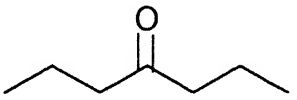
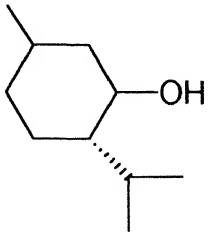
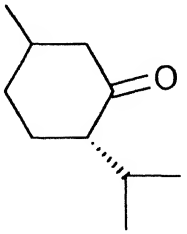
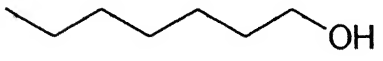


Scheme 35

Cobalt complex

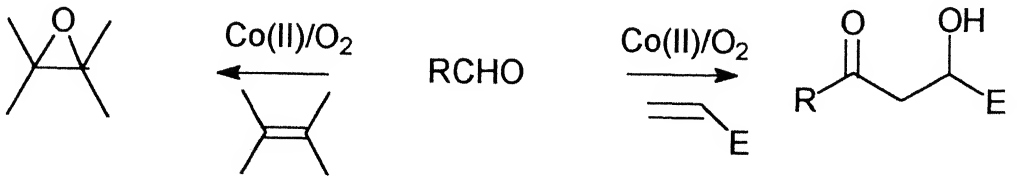
Alcohols such as benzyl alcohol and cycloheptanol are categorically transformed into the corresponding carbonyl compounds. Recently, Murahashi and coworkers[66] have reported that ruthenium-cobalt bimetallic catalyst oxidized alcohols to their corresponding ketones or acids in the presence of molecular oxygen and aldehyde (Table. 19).

Table 19. Aerobic Oxidation of Alcohols with Ruthenium-Cobalt Bimetallic Catalyst in the Presence of Acetaldehyde

Entry	Alcohol	Product	% Yield
1			89
2			95
3			96

2.2 Present Study

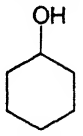
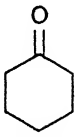
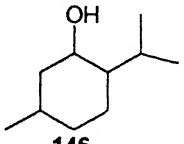
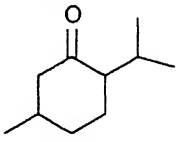
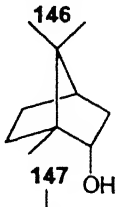
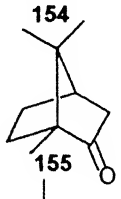
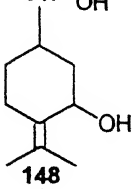
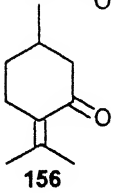
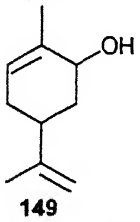
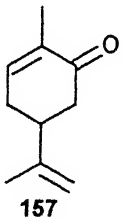
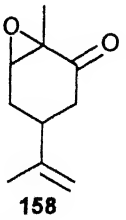
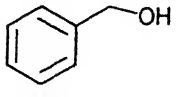
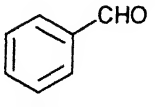
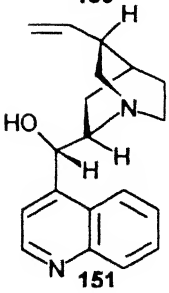
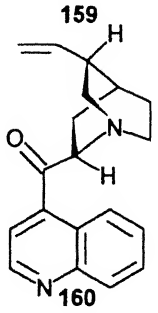
We have earlier shown that cobalt(II) Schiff base complexes act as an excellent catalysts in oxidation and oxidative addition to alkenes in the presence of enolizable aldehydes (Scheme 36). We now show here, the cobalt complex **99c** acts as an efficient catalyst in oxidizing various alcohols to the corresponding carbonyl compounds in the presence of dioxygen and 2-methylpropanal.

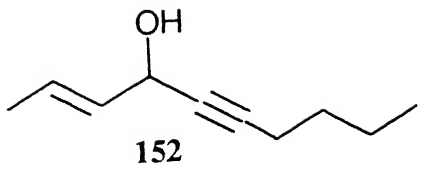


Scheme 36

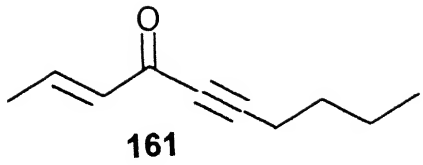
Secondary cyclic alcohols ie. cyclohexanol **145** and menthol **146** underwent smooth oxidation to the corresponding ketones in good yields. Similarly, borneol **147** was converted ..

Table 20. Cobalt(II) Catallysed Oxidation of Secondary Alcohols to Carbonyl Compounds in the Presence of Dixygen

Entry	Alcohol	Product	yield, %
1	 **145**	 **153**	79
2	 **146**	 **154**	76
3	 **147**	 **155**	70
4	 **148**	 **156**	72
5	 **149**	 **157**  **158**	(33:28) 61
6	 **150**	 **159**	82[a]
7	 **151**	 **160**	38

8 

152



161

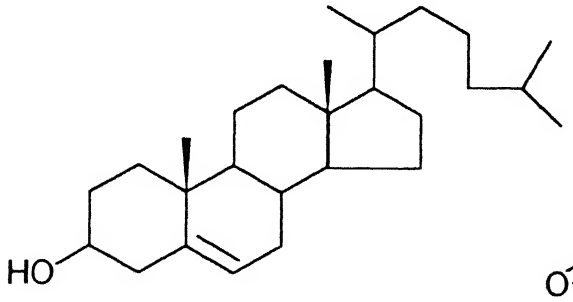
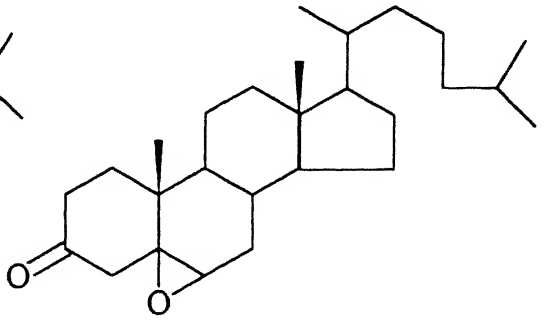
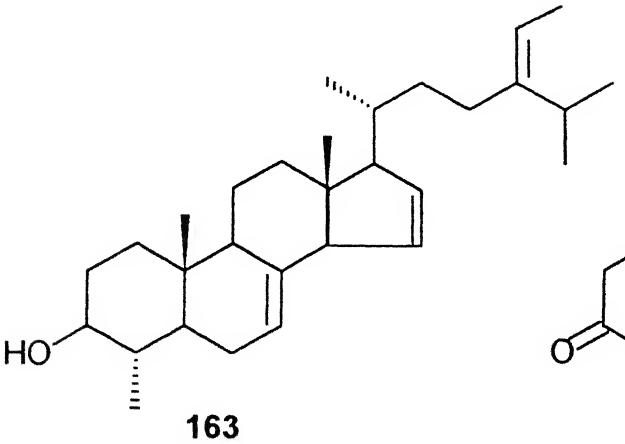
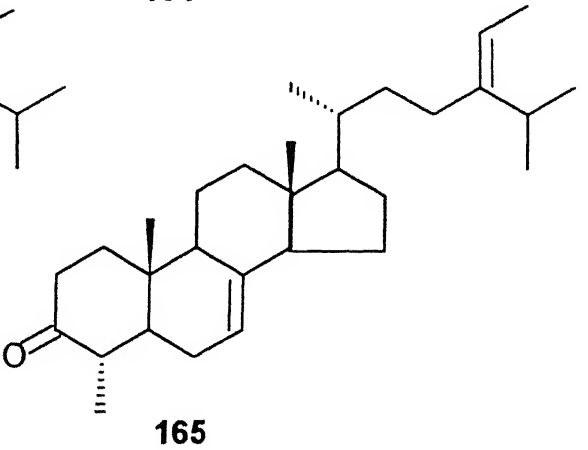
55

to camphor **155** under these conditions. The cyclic allylic alcohol p-menth-4(8)-en-3-ol **148** was oxidized to pulegone **156**, however, carveol **149** afforded mixture of carvone **157** and the corresponding epoxy ketone **158** as the major product (Table 20, Entries 4 and 5). These reaction conditions are suitable for the oxidation of benzylic alcohols as evidenced by the conversion of benzyl alcohol to benzaldehyde and cinchonine to the corresponding ketone in moderate yield (Table 20, Entries 6 and 7). The over oxidation of benzaldehyde was avoided by careful monitoring the progress of the reaction and using a limited quantity (1 equivalent) of 2-methylpropanal. The acyclic alcohol is also prone to oxidation under these conditions to afford the corresponding enone in good yield (Table 20, Entry 8).

The oxidation of cholesterol **162** in the presence of two equivalents of 2-methylpropanal **101** affords the corresponding epoxy ketone **164** as a mixture of diastereomers (Table 21, Entry 1). Surprisingly, the selective oxidation to cholestenone could not be achieved by using one equivalent of 2-methyl propanal. Interestingly, α_1-sitosterol **163** underwent selective oxidation to give the corresponding ketone **165** in good yield (Table 21, Entry 2). These reactions are facilitated by the presence of molecular sieves (4Å) which reduces the reaction time considerably. A plausible explanation for these oxidations may be given by assuming an initial formation of the cobalt superoxo-complex in the presence of aldehyde. An EPR study has indicated that the superoxo-complex is formed only when aldehyde is present in the reaction mixture (Scheme 37) and the g-value (2.0167) obtained clearly supports the formation of

monomeric superoxo species. It is conceivable that the coordination of the aldehyde to the metal will enhance the oxidisability of the latter which may lead to the formation peroxy

Table 21. Cobalt(II) Catalysed Oxidation of Secondary Alcohols with Dioxygen and 2-Methyl Propanal

Entry	Alcohol	Product	% Yield
1	 **162**	 **164**	69
2	 **163**	 **165**	57

complex. A similar observation by Basolo and coworkers[67] in related cobalt complex with different pyridine bases provides strong supports to our proposal. It is also shown recently that aldehydes facilitates the formation of metal peroxy complexes derived from nickel and cobalt. An intramolecular oxygen transfer to aldehyde via complex (a) would provide the carboxylic acid and the cobalt oxo species (b) which may subsequently oxidise the alcohol to the corresponding carbonyl compound (c) and water and in the process, the catalyst will be regenerated to complete the cycle (Scheme 37).

Cobalt(II) Catalyzed Synthesis of 1,2-Diones from Aromatic Aldehydes in the Presence of n-Butanal and Dioxygen

3.1 Introduction

Metal catalyzed oxidative coupling[6] of aldehydes is known to provide an easy access to 1,2-diones, however, it has been a relatively unexplained pathway to this type of compounds (Scheme 38). We have recently demonstrated[68] that cobalt(II) chloride catalyses the coupling

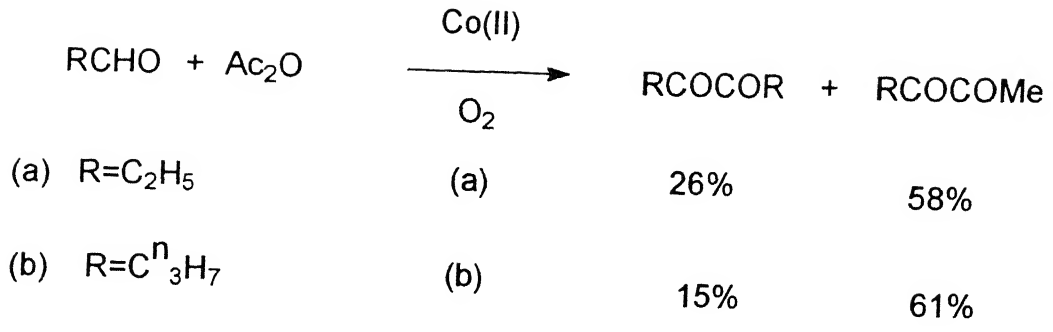
$$CH_3CHO + Mn(III) \longrightarrow CH_3C^{\cdot}O + Mn(II) + H^{+}$$

$$2CH_3C^{\cdot}O \longrightarrow CH_3COCOCH_3$$

$$CH_3C^{\cdot}O + Mn(III) \longrightarrow CH_3C^{+}O + Mn(II), \text{ etc}$$

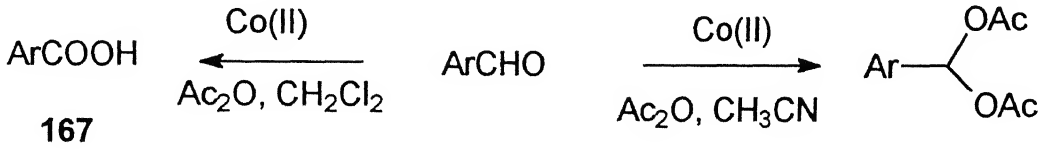
Scheme 38

of aliphatic aldehydes in the presence of acetic anhydride and dioxygen to afford 1,2-diones in good yields. A mixture of symmetrical and unsymmetrical diones were obtained with a variety of aliphatic aldehydes. A careful analysis of the reaction mixtures revealed that no acylal formation had taken place under these conditions. However, we observed the formation of the corresponding carboxylic acids in small amounts in addition to 1,2-diones. The yield of carboxylic acids were quite erratic and controlled experiments have indicated that this product



Scheme 39

arises from the oxidation of the aldehyde (Scheme 39). However, the aromatic aldehydes behaved quite differently under these conditions, and depending on the reaction medium, they were either oxidized to the corresponding carboxylic acid or underwent transformation to acylals (Scheme 40).



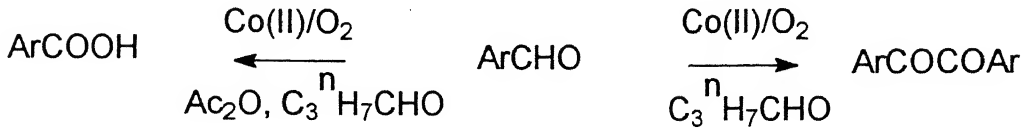
167 **168**

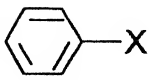
Scheme 40

3.2 Present Study

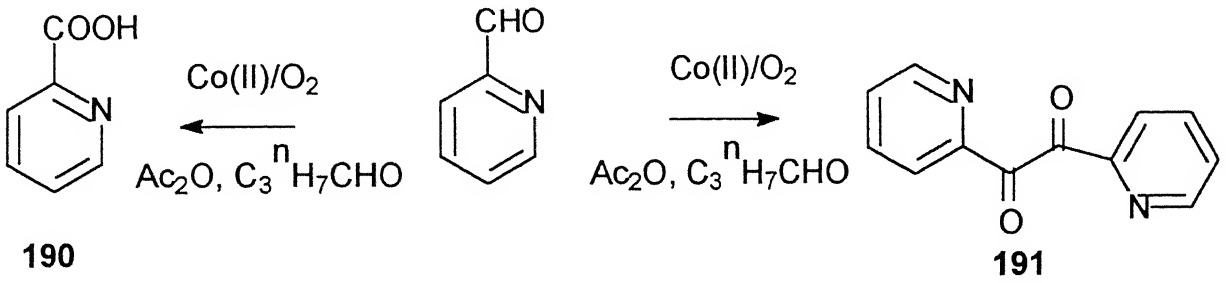
We now report that an aliphatic aldehyde (n-butanal) has an interesting effect on the reactivity of aromatic aldehydes as the latter can be transformed to the corresponding symmetrical 1,2-diones in high yields (Table 22). Thus, the reaction of aromatic aldehydes and n-butanal(1 mmol) in the presence of dioxygen and cobalt(II) chloride (5 mol%) in acetonitrile at ambient temperature afforded the corresponding 1,2-diones in high yields. It is interesting to note that the 4-substituted benzaldehyde undergo 1,2-dione formation quite readily whereas

Table 22 . Cobalt(II) Catalysed Reaction of Aromatic Aldehydes with Dioxygen in the Presence of n-Buatanal



Entry	Ar= 	Product(s) (% Yield)	
		1,2-Dione	Acid
1	X=H(**169**)	-	**182**(71)
2	F(**170**)	**177**(70)	**183**(68)
3	Cl(**171**)	**178**(81)	**183**(65)
4	Br(**172**)	**179**(65)	**184**(63)
5	CN(**173**)	**180**(33)	**185**(69)
6	Me(**174**)	**181**(52)	**186**(75)
7	OAc(**175**)	-	**187**(62)
8	OMe(**176**)	-	**188**(71)

benzaldehyde or 4-methoxybenzaldehyde mainly transformed to the corresponding carboxylic acid. Similarly, pyridinecarboxaldehyde also provides high yields of 1,2-dione and acid under these conditions (Scheme 41). Surprisingly, no 1,2-diones are observed when these reactions are carried out in the presence of three fold excess of acetic anhydride and n-butanal, instead the corresponding carboxylic acids are obtained in good yields. This difference in the behavior of the aromatic aldehydes is clearly due to the presence of n-butanal as our earlier studies have indicated that the reaction of aromatic aldehydes with excess of acetic anhydride and cobalt(II) chloride in acetonitrile afford the corresponding acylal in high yields. A non-aqueous analysis of the reaction mixture reveals that n-butanal undergoes transformation to butyric acid under these conditions and there is no observable cross or homocoupling between the two aldehydes.



190 191

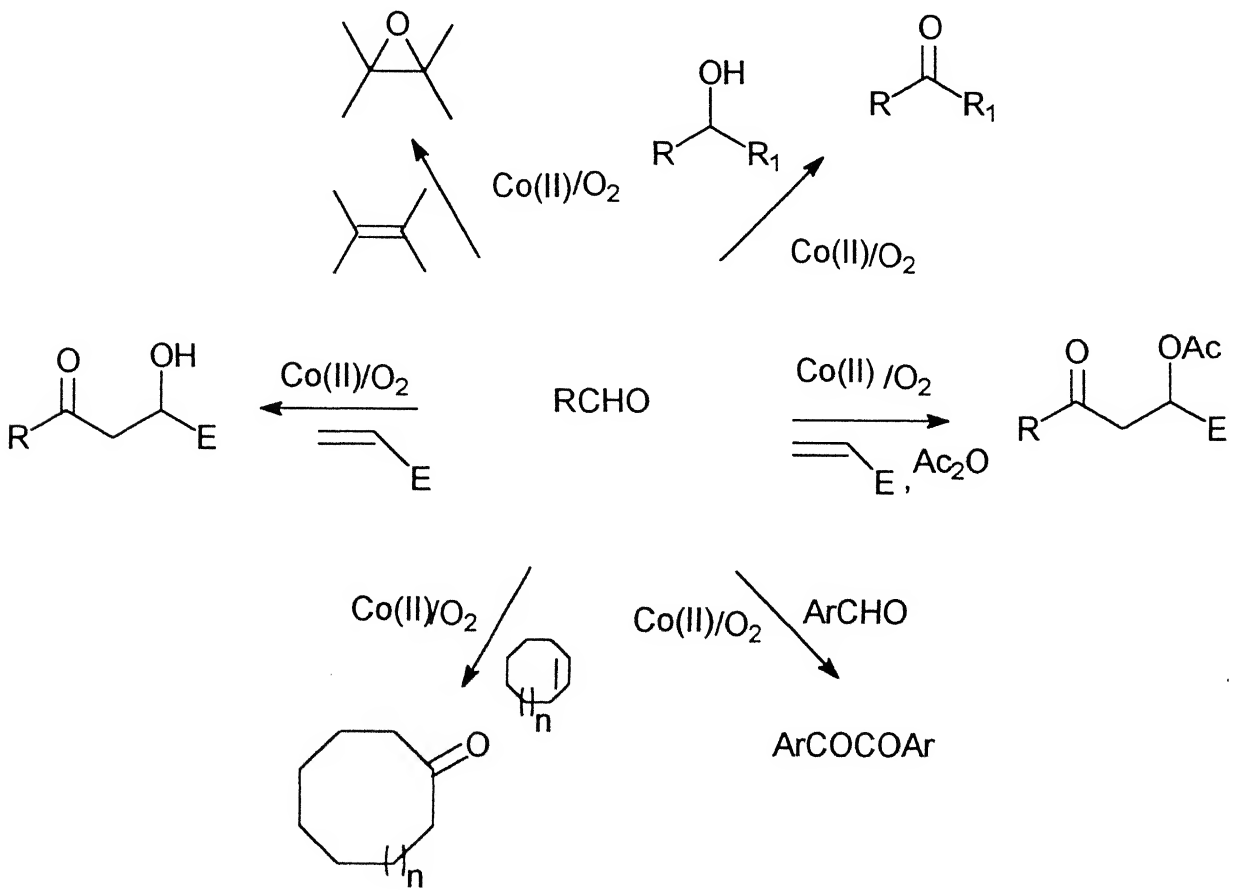
Scheme 41

However, 2-chlorobenzaldehyde, 3-chlorobenzaldehyde, 3-methoxybenzaldehyde, 2-hydroxy,3-hydroxy,4-hydroxybenzaldehydes, 4-amino benzaldehyde and 4-$(Me)_2$N-benzaldehyde did not react under these conditions, the aldehydes have been recovered without loss.

4 Conclusion

In conclusion, this part describes novel and efficient route to acyl radicals which can be transformed into useful organic products like β-hydroxy δ-ketoesters and δ-acyloxy δ-ketoesters and 1,2-diones. The acyl radical can also be used to synthesize, the highly useful synthetic intermediates, epoxides and cyclicketones in mild conditions. The mechanistic investigation has

indicated that aliphatic aldehydes are very efficient reducing agent during oxygenation of alkenes with dioxygen and cobalt(II) Schiff base catalyst. In addition, we have also shown that cobalt catalyzed oxidation of alcohols can be efficiently carried out in the presence of aldehyde and dioxygen. Further, activities in this project will involve the application of this methodology to the functionalization of hydrocarbons which is an area of current interest.



5 Experimental

5.1 General Methods and Materials

Infrared spectra were recorded on Perkin Elmer 1320 and 683 spectrometers. ^{1}H NMR spectra were recorded on Jeol PMX-60 (60 MHz), Bruker WP-80 (80 MHz) and PMX-400 (400 MHz) spectrometers in carbontetrachloride, chloroform-d and dimethylsulfoxide-d_6, the chemical shifts are reported on δ scale using tetramethylsilane as internal standard. The abbreviations s, d, t, q and m refer to singlet, doublet, triplet and multiplet respectively. Coupling constants(J), wherever mentioned have been given in Hz.

Mass spectra were recorded on JEOL SX 102/DA-6000 mass spectrometer at 70 ev. UV-VIS spectra were obtained from Perkin Elmer Lambda-2 spectrophotometer in 1,2-dichloroethane, dichloromethane and acetonitrile. EPR spectra were recorded on Varion-100 Series Spectrophotometer in acetonitrile at ambient temperature. Magnetic moment(μ_{eff}) was calculated by Evans method[69] in dichloromethane and acetonitrile. Conductivity measurements were carried out on conductivity bridge type CM82T in acetonitrile. Column chromatography was carried out using 60-120 mesh (Acme) silica gel or neutral alumina. Ethyl acetate and petroleum ether were used as the eluent. Analytical thin layer chromatography was performed on silica gel (Acme) coated glass plates using ethyl acetate and petroleum ether solvent system. High Performance Liquid Chromatography was carried out on Shimadzu LC-6A. Gas chromatography was carried out on 5765 Nucon Gas Chromatograph where nitrogen was used as carrier gas. Elemental analysis was conducted using Coleman automatic C, H and N analyzer.

Cobalt(II) chloride was purchased from Loba (India) Ltd., and it was heated to 110°C for 3h, and crushed to powder before use. Aldehydes and alkenes were obtained from Aldrich,

Fluka and E.Merck GmbH. Cis-2-octene was purchased from Phillips Petroleum Company, Oklahoma. The above materials were purified according to standard procedure prior to use. 4-Chlorobutanal was prepared according to literature[70]. Analytical reagent grade acetonitrile, acetic anhydride were obtained from BDH (India) Ltd., and purified according to the standard procedure. All the known compounds were characterized by comparing the data with literature.

5.2 Preparation of Amino Acid Ester Hydrochloride.

L-Phenylalanine Methyl Ester Hydrochloride (187).

To stirred and ice cooled dry methanol (44 ml) was added dropwise $SOCl_2$ (8.88g, 67 mmol) followed by L-phenylalanine (9g, 54.5 mmol). The reaction mixture was allowed to attain room temperature and refluxed for 2h. The solvent was evaporated and the residue, on crystallization from dry methanol-diethyl ether gave **187** (9.37g, 80%).

IR (KBr): υ_{max} 1730 cm^{-1}.

mp.: 162-163° C (lit.[71] mp. 160° C)

L-Serine Methyl Ester Hydrochloride (188).

A stirred suspension of L-serine (3.15g, 30 mmol) in dry methanol (40 ml) was subjected to a steam of dry HCl gas for 3h at ice cooled condition. During this process the product started separating as white solid. The reaction mixture was refrigerated for 4h, filtered. The residue was dissolved in dry hot methanol (25 ml) with protection from moisture, filtered, the filtrate refrigerated overnight and the resulting **188** filtered out and dried to give in 74% (3.4g) yield.

IR (KBr): υ_{max} 3380, 1730 cm^{-1}.

mp.: 166 °C (lit.[72] mp. 166° C)

L-Threonine Methyl Ester Hydrochloride (189).

L-Threonine methyl ester hydrochloride was prepared according to the above procedure to afford **189** (3.95g, 93%) as a thick liquid.

L-Methionine Methyl Ester Hydrochloride (190).

L-Methionine (5.25g, 35 mmol) was stirred in methanol (35 ml) at 0° C. $SOCl_2$ (5g, 38 mmol) was added to it drop wise. The reaction mixture was allowed to attain room temperature and stirred for overnight. Solvent was evaporated in vacuo, the residue triturated with dry ether and the resulting solid, on crystallization from dry methanol-ether gave 82% (5.73g) of **190**.

IR (KBr): υ_{max} 1730 cm^{-1}.

mp.: 152-153° C (lit.[73] mp. 151° C).

L-Histidine Methyl Ester Hydrochloride (191).

A stirred suspension of L-histidine (2.23g, 14.35 mmol) in dry methanol (28 ml) was admixed with con. H_2SO_4 (0.8 ml), refluxed for 2.5h, subjected to a dry HCl gas for 3h, the product was refrigerated for 4h, filtered. The residue dissolved in dry hot methanol (15 ml) with protection from moisture, filtered, the filtrate, refrigerated overnight and the resulting **191** filtered and dried to give in 85% (3g) yield.

IR (KBr): υ_{max} 1730 cm^{-1}.

mp.: 204-205°C (lit.[74] mp. 200-202° C).

5.3 Preparation of Schiff Base Ligands.

Salicylidene N-(phenethyl) (98a). The Schiff base ligand was prepared by the reaction of (α)-S-Methylbenzylamine (0.6g, 5 mmol) with salicylaldehyde (0.61g, 5 mmol) in absolute ethyl

alcohol (10 ml) at ambient temperature by stirring for 5h to afford **98a** (1g, 89%) as yellow powder.

^{1}H NMR ($CDCl_3$):δ 1.55 (d, 3H, J=6.5 Hz), 4.2 (q, 1H, J=6.0 Hz), 6.5-7.1 (m, 10H), 8.2 (s, 1H).

IR (KBr): υ_{max} 1620 cm^{-1}.

Anal. Calcd. for $C_{15}H_{15}ON$: C, 79.97; H, 6.70.

Found: C, 80.00; H, 6.73.

mp.: 66-67°C.

Salicylidene-N-(methyl 3-phenylpropionate) (98b). L-Phenylalanine methyl ester hydrochloride (1g, 5 mmol) was reacted with saturated sodium bicarbonate solution (pH=7) in dichloromethane at 0° C for 1h. The organic layer was separated and dried (Na_2SO_4). Removal of the solvent in vacuo afforded the free ester which was reacted with salicylaldehyde (0.6g, 5mmol) in absolute ethyl alcohol (10 mL) to afford **98b** (1.1g, 78%) as yellow oil on column chromatography (silica gel 60-120 mesh; 1:4 EtOAc/Pet. ether).

^{1}H NMR ($CDCl_3$): δ 2.55 (d, 2H, J=6.5 Hz), 3.6 (s, 3H), 4.0 (t, 1H, J=6.0 Hz), 6.4-7.0 (m, 5H), 7.1 (s, 5H), 8.2 (s, 1H).

IR ($CDCl_3$): υ_{max} 1730, 1620 cm^{-1}.

Anal. Calcd. for $C_{17}H_{17}O_3N$: C, 72.06; H, 6.04.

Found: C, 72.10; H, 6.03.

Salicylidene-N-(methyl 3-hydroxypropionate) (98c). Salicylaldehyde (0.61g, 5 mmol), L-serine methyl ester hydrochloride (0.78g, 5 mmol) and triethylamine (0.6g, 5.5 mmol) were subjected to the above reaction conditions to afford **98c** (0.86g, 77 %) as yellow oil.

^{1}H NMR ($CDCl_3$): δ 3.5 (s, 3H), 3.6-4.0 (m, 4H), 6.6-7.1 (m, 5H), 8.1 (s, 1H).

IR (neat): υ_{max} 3450, 1735 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}O_4N$: C, 59.19; H, 5.82.

Found: C, 59.14; H, 5.83.

Salicylidine-N-(Methyl 3-hydroxybutanoate) (98d). L-Threonine methyl ester hydrochloride (1.69g, 10 mmol) was reacted with dry triethylamine (1.1g, 11 mmol) in dry chloroform (25 mL). The solid was filtered and the filtrate was treated with dry diethyl ether to remove the triethylamine hydrochloride. Removal of the solvent afforded the free ester which was reacted with salicylaldehyde (1.2g, 10 mmol) in absolute ethyl alcohol (10 ml) to afford **98d** (1.66g, 70%) as red colored powder.

^1H NMR($CDCl_3$): δ 1.2 (d, 3H, J=6.5 Hz), 3.6 (s, 3H), 3.6-4.0(m, 3H), 6.6-7.2(m, 5H), 8.1 (s, 1H).

IR(KBr): υ_{max} 3450, 1730 cm^{-1}.

mp.: 148°C.

Anal. Calcd. for $C_{12}H_{15}O_4N$: C, 60.75; H, 6.32.

Found: C, 60.70; H, 6.35.

Salicylidene-N-(methyl 4-thiomethylbutanoate) (98e). L-Methionine methyl ester hydrochloride (1g, 5 mmol) and triethylamine (0.6g, 5.5 mmol) were stirred in dichloromethane (15 ml) at 0° C for 0.5h followed by at ambient temperature for 1h. Triethylamine hydrochloride was filtered and evaporation of the solvent gave the free ester which was reacted with salicylaldehyde (0.61g, 5 mmol) in absolute ethyl alcohol (10 ml) for 5h at ambient temperature. Removal of ethyl alcohol in vacuo afforded **98e** (0.93g, 70%) as brown color oil.

^1H NMR ($CDCl_3$):δ 2.0 (s, 3H), 2.05-2.5(m, 4H), 3.7 (s, 3H), 4.05 (t, 1H, J=6.0 Hz), 6.8 (d, 2H,

J=7Hz), 6.9 (s, 1H), 7.07 (d, 2H, J=6.5 Hz), 8.2 (s, 1H).

IR ($CDCl_3$): υ_{max} 1730 cm^{-1}

Anal. Calcd. for $C_{13}H_{17}O_3NS$: C, 58.42; H, 6.40.

Found: C, 58.40; H, 6.42.

Ligand 98g Derived from Acetylacetone and (L)-Histidine Methyl Ester Hydrochloride. L-(-)-Histidine methyl ester hydrochloride (1.2g, 5 mmol), triethylamine (1g, 10 mmol) and acetylacetone (0.25g, 2.5 mmol) were stirred in absolute ethyl alcohol (20 ml) for 5h at ambient temperature. The solvent was removed in vacuo and the residue was dissolved in dry acetonitrile (25 ml). The triethylamine hydrochloride was filtered and acetonitrile was removed in vacuo to give **98g** (0.7g, 69%) as a red thick liquid.

^1H NMR($CDCl_3$): δ 1.9 (s, 3H), 2.0 (s, 3H), 3.0-3.4 (m, 8H), 3.8 (s, 6H), 5.0 (s, 1H), 7.0 (s, 2H), 7.8 (s, 2H).

IR($CHCl_3$): υ_{max} 1730 cm^{-1}

Bisoxazoline (99f). This ligand was prepared according[59] to Masamune's procedure and tributyltinchloride was used as catalyst for dehydration.

1H NMR ($CDCl_3$+DMSO-d_6): δ 0.7-1.1 (m, 12H), 1.6-2.2 (m, 2H), 3.4-3.8 (m, 4H), 7.6-8.1 (m, 2H)

5.4 General Procedure for the Preparation of Cobalt(II) Chiral Complexes.

Cobalt(II) chloride and Schiff base ligand (1:2 ratio) were reacted in acetonitrile at ambient temperature for 15-17 h under nitrogen atmosphere. Removal of the solvent followed by crystallization afforded **99a-g** in good yields. The geometry of these complexes are found to

be tetrahedral.

[Bis(salicylidene-N-phenethyl)] cobalt (99a). Salicylidene-N-phenethyl **98a** (1.12g,5 mmol) and cobalt(II) chloride(0.32g, 2.5 mmol) were stirred under nitrogen atmosphere at ambient temperature for 15h. Removal of the solvent in vacuo, and crystallization in petroleum ether and dichloromethane resulted **99a** (1.0g,81%) yield as green colored powder. The geometry of the complex was found to be tetrahedral.

UV-Vis ($ClCH_2CH_2Cl$): λ_{max} 630, 666, 693 nm.

μ_{eff}: 4.5 (lit.[69,75] μ_{eff} 4.67).

Conductivity (CH_3CN): 25mΩ cm^2 mol^{-1}.

MS(m/z): 508(M^++1), 507(M^+), 283, 105(100), 77, 51.

Anal. Calcd. for $C_{30}H_{28}N_2O_2Co$: C, 71.00; H, 5.52.

Found: C, 70.98; H, 5.53.

[Bis(salicylidene-N-(methyl 3-phenylpropionate)]cobalt (99b). Salicylidene-N-(methyl 3-phenylpropionate) (1.41g,5 mmol) and cobalt(II) chloride (0.32g,2.5 mmol) were subjected to the above reaction conditions to afford **99b** (1.2g, 77%) as green colored powder.

UV-Vis (CH_2Cl_2): λ_{max} 614, 630 and 664 nm.

μ_{eff}: 4.60 (lit.[69,75] μ_{eff} 4.67).

Conductivity: 27 mΩ cm^2 mol^{-1}.

IR (CH_3CN): υ_{max} 1730 cm^{-1}

MS (m/z): 622(M^+), 621, 341(100), 283, 77, 51.

Anal. Calcd. for $C_{34}H_{32}O_6N_2Co$: C, 65.59; H, 5.14.

Found: C, 65.53; H, 5.12.

[Bis(salicylidene-N-(methyl 3-hydroxypropionate)] cobalt (99c). Salicylidene-N-(methyl 3-hydroxypropionate (1.1g, 5 mmol) and cobalt(II) chloride (0.32g, 2.5 mmol) were subjected to the above reaction conditions to afford **99c** (0.88g, 70%) as powder.

UV-Vis (CH_2Cl_2): λ_{max} 615, 632, 664 nm

IR (CH_3CN): υ_{max} 3450, 1730 cm^{-1}.

μ_{eff}: 4.55 (lit.[69,75] μ_{eff} 4.69).

MS (m/z): 503(M^+), 502, 282(100).

Anal. Calcd. for $C_{22}H_{24}O_8N_2Co$: C, 52.58; H, 4.77.

Found: C, 52.48; H, 4.78.

[Bis(salicylidene-N-(methyl 3-hydroxybutanoate)] cobalt (99d). Salicylidene-N-(methyl 3-hydroxybutanoate (1.1g,5 mmol) and cobalt(II) chloride(0.32g, 2.5 mmol) were subjected to the above reaction conditions to afford **99d** (0.95g, 72%) as green colored powder.

UV-Vis (CH_2Cl_2): λ_{max} 613, 632, 664 nm

IR (CH_3CN): υ_{max} 3500, 1730 cm^{-1}.

μ_{eff}: 4.52 (lit.[69,75] μ_{eff} 4.69).

Anal. Calcd. for $C_{24}H_{28}O_8N_2Co$: C, 54.33; H, 5.28;

Found: C, 54.31; H, 5.29.

[Bis(salicylidene-N-(methyl 4-thiomethylbutanoate)] cobalt (99e). Salicylidene-N-(methyl 4-thiomethylbutanoate (1.33g, 5 mmol) and cobalt(II) chloride (0.32g, 2.5 mmol) were subjected to the above reaction conditions to afford **99e** (0.98g, 69%) as brown colored powder.

UV-Vis (CH_2Cl_2): λ_{max} 615, 632, 664 nm

IR (CH_3CN): υ_{max} 1730 cm^{-1}.

μ_{eff}: 4.52 (lit.[69,75] μ_{eff} 4.69).

Anal. Calcd. for $C_{26}H_{32}O_6N_2S_2Co$: C, 52.88; H, 5.42.

Found: C, 52.86; H, 5.43

Coblat(II) Complex 99f Derived from Ligand 98f. Bisoxazoline **98f** (0.47g, 2 mmol) and cobalt(II) chloride (0.26g, 2 mmol) were taken in 25 ml of dry acetonitrile and subjected to the above reaction conditions to afford **98f** (0.57g, 78%) as green colored powder.

UV-Vis (CH_2Cl_2): λ_{max} 615, 630, 665 nm.

μ_{eff}: 4.52 (lit.[69,75] μ_{eff} 4.69).

Anal Calcd. for $C_{13}H_{22}O_2N_2Cl_2Co$: C, 40.68; H, 6.21.

Found: C, 39.99; H, 6.00.

Cobalt(II) Complex 99g Derived from Ligand 98g. The Schiff base ligand **98g** (0.88g, 2 mmol) and cobalt(II) chloride (0.26g, 2 mmol) were taken in 25 ml dry acetonitrile under nitrogen atmosphere and stirred for 12h at ambient temperature. The solvent was removed in vacuo, and the complex was recrystallized from acetonitrile and dichloromethane to provide **99g** (0.33g, 68%) as green colored crystals.

UV-Vis(CH_3CN): λ_{max} 684 nm.

IR (CH_3CN): υ_{max} 1730 cm^{-1}

μ_{eff}: 4.52 (lit.[69,75] μ_{eff} 4.69).

Anal. Calcd. for $C_{19}H_{24}O_4N_6Co$: C, 49.78; H, 5.24.

Found: C, 49.69; H, 5.20.

.5.5 General Procedure for the Synthesis of 2-Hydroxy and 2-Acyloxy-4-oxoesters. Aldehyde (10 mmol) and electron deficient alkene (30 mmol) were added to a stirred solution of cobalt Schiff base complex or $CoCl_2$(5 mol%) in anhydrous acetonitrile (60 ml). The reaction mixture was stirred at ambient temperature (25°C) for 20-24h. The solvent was removed in vacuo and the residue was dissolved in ether. The ether layer was successively washed with sodium bicarbonate solution (4x15 ml), water (2x20 ml) and brine (2x20 ml). Drying (Na_2SO_4) and removal of the solvent yielded a residue which was subjected to column chromatography.

Methyl 2-hydroxy-4-oxohexanoate(105a). Propanal (0.58g, 10 mmol), methyl acrylate (2.6g, 30 mmol) and cobalt(II) complex **99a** (5 mol%) were subjected to the reaction conditions as described in the general procedure to afford **105a** (0.22g, 14%) as a clear liquid by column chromatography on silica gel (60-120 mesh, 1:9 EtOAc/Pet. ether).

^{1}H NMR (CCl_4): δ 1.1 (t, 3H, J=6.0 Hz), 2.4 (q, 2H, J=6.0 Hz), 2.8 (d, 2H, J=6.0 Hz), 3.8 (s, 3H), 4.3 (t, 1H, J=6.0 Hz).

IR (neat):υ_{max} 3450, 1750, 1720 cm^{-1}.

Anal. Calcd. for $C_7H_{12}O_4$: C, 52.49; H, 7.55.

Found: C, 52.51; H, 7.54.

Methyl 2-hydroxy-5-methyl-4-oxohexanoate(105b). Isobutanal (0.72g, 10 mmol), methyl acrylate (2.6g, 30 mmol) and cobalt(II) complex **99a** (5 mol%) were subjected to the above reaction conditions to give **105b** (0.295g, 17%) as an oil.

^{1}H NMR (CCl_4):δ 1.0 (d, 6H, J=6.5 Hz), 2.1-2.7(m, 1H), 2.8 (d, 2H, J=7.0 Hz), 3.8 (s, 3H), 4.2 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 3450, 1750, 1720 cm^{-1}.

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.15; H, 8.10.

Found: C, 55.10; H, 8.11

Methyl 2-hydroxy-4-oxoheptanoate (105c). n-Butanal (0.72g, 10 mmol), methyl acrylate (2.6g, 30 mmol) and cobalt(II) complex **99a** (5 mol%) were subjected to the above reaction conditions to provide **105c** (0.31g, 18%) as colorless oil.

^{1}H NMR (CCl_4): δ 1.0 (t, 3H, J=6.0 Hz), 1.2-1.8(m, 2H), 2.35 (t, 2H, J=6.0 Hz), 2.8 (d, 2H, J=6.5 Hz), 3.7 (s, 3H), 4.1 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 3450, 1750, 1720 cm^{-1}.

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.15; H, 8.10.

Found: C, 55.17; H, 8.11.

Methyl 2-hydroxy-7-chloro-4-oxoheptanoate (105d). 4-Chlorobutanal (0.53g, 5 mmol), methyl acrylate (1.33g, 15 mmol) and **99a** (5 mol%) were subjected to the reaction conditions as described in the above procedure to afford **105d** (0.17g, 17%) as an oil.

^{1}H NMR (CCl_4): δ 1.2-1.4(m, 2H), 1.9-2.1(m, 2H), 2.45 (d, 2H, J=6.0 Hz), 3.5(s, 3H), 4.0-4.1 (m, 3H), 4.95 (t, 1H, J=6.0 Hz)

IR (neat): υ_{max} 3450, 1720 cm^{-1}.

Anal. Calcd. for $C_8H_{13}O_4Cl$: C, 46.15; H, 6.25.

Found: C, 46.11; H, 6.26

2-Hydroxy-5-methyl-4-oxohexanenitrile (105f). 2-Methylpropanal (0.72g, 10 mmol), acrylonitrile (1.59g, 30 mmol) and cobalt(II) chloride (5 mol%) were reacted as described in the procedure to yield **105f** (0.35g, 25%) as a liquid.

^{1}H NMR (CCl_4): δ 1.1 (d, 6H, J=6.5 Hz), 2.2-2.75 (m, 1H), 2.95 (d, 2H, J=6.5 Hz), 4.7 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 3460, 2260, 1710 cm^{-1}.

Anal. Calcd. for $C_7H_{11}O_2N$: C, 59.57; H, 7.80.

Found: C, 59.52; H, 7.82.

Methyl 2-propionoxy-4-oxohexanoate (106a). Propanal (0.58g, 10 mmol), methyl acrylate (2.6g, 30 mmol) and cobalt(II) complex **99a** (5 mol%) were carried out according to the procedure described in the above procedure for 15h. Usual workup followed by column chromatography on silica gel (1:19 EtOAC/Pet. ether) afforded **106a** (0.49g, 23%) as an oil.

^{1}H NMR (CCl_4): δ 0.95 (t, 3H, J=6.0 Hz), 1.10 (t, 3H, J=6.0 Hz), 2.10 (q, 2H, J=6.0 Hz), 2.30 (q, 2H, J=6.0 Hz), 2.75 (d, 2H, J=6.0 Hz), 3.6 (s, 3H), 5.15 (t, 1H, J=6.0 Hz).

MS (m/z): 217(M^++1), 216(M^+), 153, 143, 73, 57(100), 29, 15.

IR (neat): υ_{max} 1750, 1720 cm^{-1}.

Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.52; H, 7.40.

Found: C, 55.53; H, 7.42.

Methyl 5-Methyl-2-isobutyryloxy-4-oxohexanoate (106b). Isobutanal (0.72g, 10 mmol), methyl acrylate (2.6g, 30 mmol) and cobalt(II) complex **99a** (5 mol%) were subjected to the above reaction conditions to give **106b** (0.51g, 21%) as colorless oil.

^{1}H NMR (CCl_4): δ 0.8 (d, 6H, J=6.5 Hz), 1.0 (d, 6H, J=6.5 Hz), 2.1-2.8 (m, 2H), 2.9 (d, 2H, J=6.0 Hz), 3.8 (s, 3H), 5.6 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 1750, 1720 cm^{-1}.

Anal. Calcd. for $C_{12}H_{20}O_5$: C, 58.99; H, 8.20.

Found: C, 59.02; H, 8.23

Methyl 2-butyryloxy-4-oxoheptanoate(106c). n-Butanal (0.72g, 10 mmol), methyl acrylate (2.6g, 30 mmol) and cobalt(II) complex **99a** (5 mol%) were reacted as described above to give **106c** (0.46g, 19%) as an oil.

^{1}H NMR (CCl_4): δ 0.8 (t, 3H, J=6.0 Hz), 1.0 (t, 3H, J=6.0 Hz), 1.2-1.8 (m, 4H), 2.1 (t, 2H, J=6.0 Hz), 2.35 (t, 2H, J=6.0Hz), 2.8 (d, 2H, J=6.0 Hz), 3.6 (s, 3H), 5.2 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 1750, 1720 cm^{-1}.

Anal. Calcd. for $C_{12}H_{20}O_5$: C, 58.99; H, 8.20.

Found: C, 59.04; H, 8.22.

Methyl2-(4-chlorobutyryloxy)-7-chloro-4-oxoheptanoate(106d). 4-Chloro butanal (1g, 10mmol), methyl acrylate (2.6g, 30 mmol) and **99a** (5 mol%) were subjected to the above reaction conditions to afford **106d** (0.74g, 24%) as an oil.

^{1}H NMR (CCl_4): δ 1.2-1.8 (m, 4H), 1.8-2.2 (m, 4H), 2.9 (d, 2H, J=6.0 Hz), 3.7 (s, 3H), 4.0-4.1 (m, 4H), 4.8-5.1 (t, 1H, J=6.0 Hz)

IR (neat): υ_{max} 3450, 1720 cm^{-1}.

Anal. Calcd. for $C_{12}H_{18}O_5Cl_2$: C, 46.15; H, 5.76.

Found: C, 46.19; H, 5.79

2-Propionoxy-4-oxohexane nitirle (106f). Propanal (0.58g, 10 mmol), acrylonitrile (1.59g, 30 mmol) and **99a** (5 mol%) were treated as described in the above procedure to give **106f** (0.21g, 11%) as an oil.

^{1}H NMR (CCl_4): δ 1.0 (t, 6H, J=6.0 Hz), 2.2-2.6 (m, 4H), 2.85 (d, 2H, J=6.0 Hz), 5.5 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 2260, 1740, 1710 cm^{-1}.

Anal. Calcd. for $C_9H_{13}O_3N$: C, 59.02; H, 7.10.

Found: C, 59.00; H, 7.13.

5.6 General Procedure for the Synthesis of 2-Acetoxy-4-oxoesters. Aldehyde (10 mmol), electron deficient alkene (30 mmol) and acetic anhydride (30 mmol) were added to a stirred solution of cobalt(II) chloride or cobalt(II) Schiff base complex (~5 mol %) in anhydrous acetonitrile (60 ml). The mixture was stirred at ambient temperature (25°C) for 20-24h. The usual workup followed by column chromatography afforded the acetoxy compounds in good yields.

Methyl 2-acetoxy-5-methyl-4-oxohexanoate (107a). Isobutanal (0.72g, 10 mmol), methyl acrylate (2.6g, 30 mmol), acetic anhydride (3g, 30 mmol) and cobalt(II) chloride (5 mol%) were subjected to the reaction conditions as described in the general procedure to afford **107a** (1.7g, 77%) as an oil.

^{1}H NMR (CCl_4): δ 1.0 (d, 6H, J=7.0 Hz), 1.9 (s, 3H), 2.1-2.6 (m, 1H), 2.75 (d, 2H, J=6.0 Hz), 3.55 (s, 3H), 5.1 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 1750, 1720 cm^{-1}.

Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46.

Found: C, 55.53; H, 7.48.

Methyl 2-acetoxy-7-chloro-4-oxoheptanoate (107b). 4-Chlorobutanal (0.53g, 5 mmol), methyl acrylate (1.3g, 15 mmol), acetic anhydride (1.5g, 15 mmol) and cobalt(II) chloride (5 mol%) were subjected to the reaction conditions as described in the general procedure to give **107b** (0.7g, 56%) as an oil on column chromatography (1:19 EtOAc/Pet. ether).

^{1}H NMR(CCl_4) δ 1.6-2.2(m, 4H), 2.0(s, 3H), 2.3-2.7(d, 2H, J=6.5 Hz), 3.5(s, 3H), 4.0(t, 2H, J=6.0 Hz), 5.0(t, 1H, J=6.0 Hz)

IR (neat): υ_{max} 1750, 1720 cm^{-1}.

Anal. Calcd. for $C_{10}H_{15}O_5Cl$: C, 48.00; H, 6.00.

Found: C, 47.98; H, 6.01.

Methyl 2-acetoxy-4-cyclohexyl-4-oxobutanoate (107c). Cyclohexanecarboxaldehyde (0.56g, 5 mmol), methyl acrylate (1.3g, 15 mmol), acetic anhydride (1.5g, 5 mmol) and cobalt(II) chloride (5 mol%) were subjected to the reaction conditions as described in the general procedure to give **107c** (0.7g, 55%) as an oil on column chromatography (1:19 EtOAc/Pet. ether).

^{1}H NMR (CCl_4): δ 1.0-3.0(m, 16H), 3.6(s, 3H), 5.0(t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 1750, 1720 cm^{-1}.

Anal. Calcd. for $C_{13}H_{20}O_5$: C, 60.93; H, 7.81.

Found: C, 60.90; H, 7.83.

2-Acetoxy-4-oxohexanenitrile (107d). Propanal (0.58g, 10 mmol), acrylonitrile (1.59, 30 mmol), acetic anhydride (3g, 30 mmol) and cobalt(II) chloride (5 mol%) were subjected to the above reaction conditions to give **107d** (0.98g, 58%) as a clear liquid.

^{1}H NMR ($CDCl_3$): δ 0.9(t, 3H, J=6.0 Hz), 2.0(s, 3H), 2.4(q, 2H, J=6.0 Hz), 2.9(d, 2H, J=6.0 Hz), 5.5(t, 1H, J=6.0 Hz).

IR (neat):υ_{max} 2260, 1740, 1720 cm^{-1}.

Anal. Calcd. for $C_8H_{11}O_3N$: C, 56.80; H, 6.50.

Found: C, 56.78; H, 6.52.

2-Acetoxy-5-methyl-4-oxohexanenitrile (107e). Isobutanal (0.72g, 10 mmol), acrylonitrile (1.53g, 30 mmol), acetic anhydride (3g, 30 mmol) and cobalt(II) chloride (5 mol%) were reacted to above reaction conditions to yield **107e** (1g, 56%) as an oil.

^1H NMR (CCl_4): δ 1.1 (d, 6H, J=6.5 Hz), 2.0 (s, 3H), 2.25-2.75 (m, 1H), 2.95 (d, 2H, J=6.0 Hz), 5.5 (t, 1H, J=6.0 Hz).

IR (neat):υ_{max} 2260, 1740, 1720 cm^{-1}.

Anal. Calcd. for $C_9H_{13}O_3N$: C, 59.02; H, 7.10.

Found: C, 59.00; H, 7.12.

2-Acetoxy-4-oxoheptanenitrile (107f). n-Butanal (0.72g, 10 mmol), acrylonitrile (1.53g, 30 mmol), acetic anhydride (3g, 30 mmol) and cobalt(II) chloride (5 mol%) were subjected to the reaction conditions as described above for 22h to afford **107f** (0.96g, 53%) as a liquid.

^1H NMR (CCl_4):δ 0.7-1.2 (m, 5H), 2.0 (s, 3H), 2.3 (t, 2H, J=6.0 Hz), 2.8 (d, 2H, J=6.5 Hz), 5.3 (t, 1H, J=6.5 Hz).

IR (neat):υ_{max} 2260, 1740, 1720 cm^{-1}.

Anal. Calcd. for $C_9H_{13}O_3N$: C, 59.02; H, 7.10.

Found: C, 59.00; H, 7.13.

5.7 General Procedure for Acylation of Allylic Alcohols. [76]

Alcohol (10 mmol), triethylamine (15 mmol), acetic anhydride (15 mmol) and DMAP (catalytic) were stirred at

room temperature for 15-16h. The reaction mixture was quenched with 5% hydrochloric acid, and extracted with diethyl ether (2X25 ml). The organic layer was washed with sodium bicarbonate solution (3x20 ml), water (2x15 ml), brine (2x15 ml). Drying (Na_2SO_4) and evaporation of the solvent gave a residue which was purified on column chromatography or Khugelror distillation.

3-Acetoxy-3,7-dimethyl-1,6-octadiene (115). 3-Hydroxy-3,7-dimethyl-1,6-octadiene (1.54g, 10 mmol), triethylamine (1.5g, 15 mmol), acetic anhydride (1.5g, 15 mmol) and DMAP (catalyst) were reacted as described in the general procedure for 15h to afford **123** (1.67g, 85%) as an oil by column chromatography (1:19 EtOAc/Pet. ether).

^{1}H NMR (CCl_4): δ 1.5 (s, 3H), 1.55 (s, 3H) 1.6 (s, 3H), 1.9 (m, 4H), 2.0 (s, 3H), 5.0 (m, 3H), 5.5-6.1 (m, 1H).

IR(neat): υ_{max} 1730 cm^{-1}.

1-Acetoxy-3,7-dimethylocta-2,6-diene (88). 1-Hydroxy-3,7-dimethyl octa-2,6-diene (0.77g, 5 mmol), acetic anhydride (0.75g, 7.5 mmol), triethylamine (0.75g, 7.5 mmol) and DMAP (catalyst) were subjected to the above reaction conditions to afford **88** (0.76g, 76%) as a liquid.

^{1}H NMR (CCl_4): δ 1.6 (s, 9H), 1.8-2.1 (m, 7H), 4.4 (d, 2H, J=6.5 Hz), 4.9-5.3 (m, 2H).

IR (neat):υ_{max} 1730 cm^{-1}.

Cholesteryl acetate (127). Cholesterol (0.39g, 1 mmol), acetic anhydride (0.15g, 1.5 mmol), triethylamine (0.15g, 1.5 mmol) and DMAP (catalyst) were stirred in dichloromethane (5 ml) for 16 h according to the procedure described in the general procedure. The usual workup and purification on column chromatography afforded **127** (0.36g, 80%) powder.

^{1}H NMR ($CDCl_3$): δ 0.7-1.0(m, 15H), 1.1-2.0(m, 29H), 2.06 (s, 3H), 4.75 (m, 1H), 5.3 (m, 1H).

IR (KBr): υ_{max} 1730 cm^{-1}.

mp.: 117-118° C.

Farnesyl acetate (118). Farnesol (2.22g, 10 mmol), acetic anhydride (3g, 30 mmol), triethylamine(3g, 30 mmol) and DMAP (catalyst) were subjected to the above reaction conditions to afford **118** (2g, 79%) as a liquid.

^{1}H NMR (CCl_4): δ 0.9 (s, 6H), 1.5 (s, 3H), 1.6 (s, 3H), 1.9-2.2 (m, 11H), 4.3-4.5 (d, 2H, J=6.0 Hz), 4.9-5.5 (m, 3H)

IR (neat):υ_{max} 1730 cm^{-1}.

5.8 General Procedure for the Synthesis of Epoxides. Aldehydes (10 mmol) and unactivated alkenes (5 mmol) were added to a stirred solution of cobalt(II) catalysts (~20 mg) in acetonitrile. The reaction mixture was stirred at room temperature under dioxygen balloon for 20-24h. The solvent was removed in vacuo, and the residue was dissolved in diethyl ether. The usual workup followed by column chromatography purification afforded the epoxides in good to high yield.

trans-Stilbene oxide (120). trans-Stilbene (0.9g, 5 mmol), 2-methylpropanal (0.72g, 10 mmol) and **99c** were subjected to the reaction conditions as described in the general procedure for 17h. Removal of the solvent followed by column chromatography purification afforded **120** (0.76g, 77%) as white crystalline solid.

^{1}H NMR (CCl_4): δ 3.7 (s, 2H), 7.0 (m, 10H).

IR (CCl_4):υ_{max} 1375, 1250 cm^{-1}.

mp.: 69°C.

Dodecene oxide (119). Dodecene (0.84g, 5 mmol), 2-methylpropanal (0.72g, 10 mmol) and cobalt(II) complex **99c** (5 mol%) under the reaction conditions described above gave **119** (0.5g, 55%) as a liquid on flash column chromatography.

^{1}H NMR (CCl_4): δ 0.85 (t, 3H, J=6.0 Hz), 1.2 (m, 18H), 2.0-2.7(m, 3H).

IR (CCl_4): υ_{max} 1375, 1250 cm^{-1}.

3-Acetoxy-3,7-dimethyl-6,7-epoxy-1-octene(123). 3-Acetoxy-3,7-dimethyl-oct-1,6-diene (0.49g, 2.5 mmol) and isobutanal (0.36g,5 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the reaction conditions as described in the general procedure to give **123** (0.44g, 84%) as a liquid.

^{1}H NMR ($CDCl_3$): δ 1.1 (s, 3H), 1.2 (s, 3H), 1.6 (s, 3H), 1.6-2.0(m, 4H), 2.0 (s, 3H), 2.4 (t, 1H, J=6.5 Hz), 4.8-5.2(m, 2H), 5.45-6.0(m, 1H).

IR (neat):υ_{max} 1725, 1360, 1240 cm^{-1}.

Anal. Calcd. for $C_{12}H_{20}O_3$: C, 73.40; H, 10.20.

Found: C, 73.44; H, 10.21.

1-Acetoxy-3,7-dimethyl-6,7-epoxoct-1-ene(124). Geranyl acetate (0.49g, 2.5 mmol) and 2-methylpropanal (0.36g, 5 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the reaction conditions as described in the general procedure to give **88c** (0.34g, 66%) as a liquid.

^{1}H NMR ($CDCl_3$): δ 1.1 (s, 3H), 1.2 (s, 3H), 1.6-1.9(m, 5H), 2.0 (s, 3H), 2.0-2.35(m, 2H), 2.8 (t, 1H, J=6.0 Hz), 4.55 (d, 2H, J=6.0 Hz), 5.35(t, 1H, J=6.5 Hz).

IR (neat):υ_{max} 1725, 1360, 1240 cm^{-1}.

Anal. Calcd. for $C_{12}H_{20}O_3$: C, 67.92; H, 9.43.

Found: C, 67.88; H, 9.45.

2,3-Epoxy carvyl acetate (125). Carvyl acetate (0.97g, 5 mmol), 2-methylpropanal (0.72g, 10 mmol) and cabalt(II) complex **99c** under the above reaction conditions afforded **125** (0.54g, 52%) as an oil.

^{1}H NMR (CCl_4): δ 0.7 (m, 5H), 1.15 (s, 3H), 1.6 (s, 3H), 2.0 (s, 3H), 2.8 (t, 1H, J=6.0 Hz), 4.55 (m, 3H),

IR(neat): υ_{max} 1730, 1360, 1240 cm^{-1}.

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.58; H, 8.57.

Found: C, 68.61; H, 8.59.

10,11-epoxyFarnesyl acetate (126). Farnesyl acetate (0.53g,2 mmol), isobutanal (0.3g,4 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the above reaction conditions for 20h to give **126** (4g, 71%) as an oil.

^{1}H NMR (CCl_4): δ 0.9 (s, 6H), 1.5 (s, 3H), 1.6 (s, 3H), 1.9-2.2 (m, 11H), 2.55 (t, 1H, J=6.0 Hz), 4.4 (d, 2H, J=6.0 Hz), 4.9-5.5 (m, 2H).

IR (neat): υ_{max} 1720, 1365, 1230 cm^{-1}.

Anal. Calcd. for $C_{15}H_{28}O_3$: C, 72.85; H, 10.00.

Found: C, 72.51; H, 10.07.

5,6-Epoxy cholesteryl acetate (129). Cholesteryl acetate (0.42g, 1 mmol), 2-methylpropanal (0.15g, 2 mmol) and cobalt(II) complex (5 mol %) in 1,2-dichloroethane and acetonitrile (1:4, 20 ml) under the above reaction conditions gave **129** (0.36g, 81%) as a mixture of two

diastereomers α:β (76:26).

^{1}H NMR ($CDCl_3$): δ 0.7-1.0(m, 15H), 1.1-2.0(m, 28H), 2.06(s, 3H), 2.45-2.64(m, 1H), 4.75(m, 1H).

IR (KBr): υ_{max} 1720, 1360, 1240 cm^{-1}.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.03; H, 11.21.

Found: C, 77.87; H, 11.19.

mp.: α, 102°C, β, 112°C.

5,6-Epoxy α_1-sitosterol acetate (130). α_1-Sitosterol acetate (0.47g, 1 mmol), isobutanal (0.2g, 3 mmol) and cobalt(II) complex **99c** (5 mol%) were reacted in 1,2-dichloroethane and acetonitrile (1:5; 25 ml) for 24h. Workup followed by column chromatography (silica gel 60-120 mesh, 5:19 EtOAc/petroleum ether) afforded **130** (0.27g, 55%) as a mixture of diastereomers.

^{1}H NMR ($CDCl_3$): δ 0.6-2.0(m, 46H), 2.05(s, 3H), 2.83-3.16(m, 1H), 4.7-5.2(m, 2H).

IR (KBr): υ_{max} 1720, 1370, 1260 cm^{-1}.

Anal. Calcd. for $C_{32}H_{52}O_3$: C, 79.33; H, 10.74.

Found: C, 79.29; H, 10.75.

mp.: 178° C.

5.9 General Procedure for the Synthesis of Allylic alcohol and Cyclic Ketones.

Cyclic alkene (5 mmol), 2-methylpropanal (10 mmol) and cobalt(II) complex (5 mol%) were stirred at ambient temperature for 30-35h using dioxygen balloon in acetonitrile. The solvent was removed in vacuo, and the residue was dissolved in diethyl ether. The organic layer was washed with $NaHCO_3$ solution (4 x 25 ml), water (2 x 15) and brine (1 x 20 ml). Drying (Na_2SO_4) and evaporation of the solvent in vacuo, resulted the residue which was purified by

distillation.

Reaction with Cyclohexene (74). Cyclohexene (0.82g, 10 mmol), propanal (1.2g, 20 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the above reaction conditions described in the general procedure for 30h to afford a mixture of compounds **83, 84** and **116** in the ratio of 1:2:0.5 in 62% yield. The product ratio was determined by gas chromatography.

Reaction with Cycloheptene (131). Cycloheptene (0.48g, 5 mmol), 2-methylpropanal (078g, 10 mmol) and cobalt(II) complex **99c** (5 mol%) under the above reaction conditions for 30h gave a mixture of compounds **136** and **137** (2:3) in 67% yield. The product ratio was determined by gas chromatography.

Cyclohept-2-enone (136).

^{1}H NMR ($CDCl_3$): δ 1.5-2.0 (m, 4H), 2.20-2.3 (m, 4H), 6.0 (m, 1H,), 6.7(m, 1H).

IR (neat): υ_{max} 1710, 1660 cm^{-1}.

Cycloheptanone (137).

^{1}H NMR ($CDCl_3$): δ 1.0-1.8 (m, 8H), 2.49 (m, 4H)

IR (neat): υ_{max} 1700 cm^{-1}.

Cyclooctanone (138). Cyclooctene (0.55g, 5 mmol), 2-methylpropanal (0.72g, 10 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the above reaction conditions for 32h to afford **138** (0.42g, 67%) as a liquid.

^{1}H NMR (CCl_4): δ 1.2-1.7 (m, 6H), 1.7-2.0 (m, 4H), 2.4 (m, 4H).

IR (neat): υ_{max} 1795 cm^{-1}.

Cyclododecanone (139). Cyclododecene (0.83g,5 mmol), 2-methylpropanal (0.72, 10 mmol) and cobalt(II) complex (5 mol%) were subjected to the above reaction conditions for 35h to yield **139** (0.56g, 62%) as a liquid.

^1H NMR (CCl_4): δ 1.2-1.7(m, 14H), 1.7-2.0(m, 4H), 2.4 (m, 4H).

IR (neat): υ_{max} 1700 cm^{-1}

Compound (140). (+)-Longifolene (0.41g, 2 mmol), 2-methylpropanal (0.36g, 5 mmol) and cobalt(II) complex **99c** (5 mol%) were reacted to the above reaction conditions for 37h to give **140** (0.31g, 65%) as a liquid .

^1H NMR ($CDCl_3$): δ 0.8 (s, 3H), 0.9 (s, 3H), 1.0 (s, 3H), 1.0-1.78(m, 10H), 1.9-2.12(m, 2H), 2.2-2.6(m, 1H), 11.0 (s, 1H).

IR ($CDCl_3$):υ_{max} 3400, 1680 cm^{-1}.

MS (m/z): 235(M^+), 219, 191, 135, 109, 81, 55, 41, 29.

Anal. Cacd. for $C_{15}H_{23}O_2$: C, 76.47; H, 9.77.

Found: C, 76.53; H, 9.79.

5.10 Preparation of Secondary Alcohols.

Alcohols were commercially purchased or prepared by $NaBH_4$ reduction and purified prior to use by distillation or crystallization.

2-Ene-4-hydroxy-5-enyne-decane. To a stirred solution of 1-hexyne (0.41g, 5 mmol) in dry THF, n-butyllithium (2.5M solution in hexane, 6 mmol) was added at ~-20°C. Reaction mixture

was stirred for 0.5h at this temperature and then stirred at room temperature for 0.5h. Crotonaldehyde (0.42g, 6 mmol) in THF was added dropwise to the reaction mixture at 0° C and stirred for 1h. The reaction mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate (3x25 ml). The organic layer was successively washed with saturated NH_4Cl solution (2x15 ml) and brine (2x15 ml). Drying (Na_2SO_4) and evaporation of the solvent gave a yellow colored thick liquid which was purified by column chromatography.

^1H NMR (CCl_4): δ 0.5-1.9(m, 7H), 1.8 (d, 3H, J=7.0 Hz), 3.1-3.5(m, 2H), 4.4-4.6(m, 1H), 5.5-5.8 (m, 2H).

IR (neat): 3460 cm^{-1}.

5.11 General Procedure for the Oxidation of Secondary Alcohols to Carbonyl Compounds.

Secondary alcohol (5 mmol), 2-methylpropanal (10 mmol) and cobalt(II) Schiff base complex (5 mol%) were stirred at ambient temperature for 15-20h using dioxygen balloon in acetonitrile solvent. The solvent was removed in vacuo, and the residue was dissolved in diethyl ether (50 ml). The organic layer was washed with sodium bicarbonate solution (4x15 ml) and brine (3x15 ml). Drying (Na_2SO_4) and removal of the solvent gave the crude compound, which was purified by distillation/column chromatography.

Menthone (154). (1S,2R,5S)-(+)-Menthol (0.78g,5 mmol), 2-methylpropanal (0.72g, 10 mmol) and cobalt(II) complex **99a** (5 mol%) were reacted according to the above procedure for 15h to afford **154** (0.58g, 76%) as an oil yield on column chromatography (1:19 EtOAc/Pet. ether).

^1H NMR($CDCl_3$): δ 0.7-1.0(m, 10H), 1.0-2.42(m, 9H).

IR ($CDCl_3$):υ_{max} 1714 cm^{-1}.

Camphor (147). Borneol (0.77g, 5 mmol), 2-methylpropanal (0.72g, 10 mmol) and cobalt(II) catalyt **99c** under the above reaction conditions provided **147** (0.53g, 70%) as solid.

^{1}H NMR($CDCl_3$): δ 0.8 (s, 3H), 0.9 (s, 3H), 1.0 (s, 3H), 1.4-1.8(m, 7H), 2.0 (d, 2H, J=6.5 Hz).

IR($CDCl_3$):υ_{max} 1720 cm^{-1}.

mp.: 178-179° C.

Benzaldehyde (150). Benzylalcohol (0.5g, 5 mmol), 2-methylpropanal (0.36g, 5 mmol) and cobalt(II) complex **99c** (5 mol%) were stirred at ambient temperature for 3h under dioxygen balloon in acetonitrile solvent. Solvent was removed in vacuo, and the residue was dissolved in diethyl ether. The organic layer was successively washed with water (2x20 ml) and brine (2X20 ml) . Drying (Na_2SO_4) and removal of the solvent in vacuo yielded crude compound which was subjected to HPLC. Yield is 82%.

^{1}H NMR (CCl_4): δ 6.8-7.1 (m, 5H), 9.0 (s, 1H).

IR (neat): υ_{max} 1685 cm^{-1}

Compound 160. The reaction of cinchonine (0.59g, 2 mmol) with 2-methylpropanal (0.36g, 5 mmol) in the presence of cobalt(II) complex **99c** (5 mol%) in 20h gave **160** (0.22g, 38%) as yellow colored solid on column chromatography (1:19 EtOAc/Pet. ether).

^{1}H NMR ($CDCl_3$): δ 1.8-2.3(m, 5H), 2.6 (m, 1H), 2.8-3.1(m, 4H), 3.6 (t, 1H, J=6.0 Hz), 5.0-5.1 (m, 2H), 5.8-6.2(m, 1H), 7.6-8.1(m, 6H).

IR ($CDCl_3$): υ_{max} 1695 cm^{-1}.

Anal. Calcd. for $C_{19}H_{20}N_2O$: C, 76.51; H, 6.81.

Found: C, 76.41; H, 6.99.

mp.: 247-249° C.

2-Ene-4-oxo-5-enyne-decane(161). 2-Ene-4-hydroxy-5-enyne-decane (0.76g,5 mmol) reacts with 2-methylpropanal (0.72g, 10 mmol) in the presence of cobalt(II) complex **99c** (5 mol%) in 24h to give **161** (0.41g, 55%) as an oil.

^{1}H NMR (CCl_4): δ 0.9 (t, 3H, J=6.0 Hz), 1.0-1.7 (m, 4H), 2.0 (d, 3H, J=6.5 Hz), 2.25 (t, 2H, J=6.0 Hz), 6.0 (d, 1H, J=13.0 Hz), 6.6-7.2 (dq, 1H, J=6.5 Hz, J=13.0 Hz).

IR (neat): υ_{max} 2200, 1730, 1640 cm^{-1}.

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.00; H, 11.66.

Found: C, 80.07; H, 11.69.

2,3-Epoxy Carvone (158). Carveol (0.76g, 5 mmol), 2-methylpropanal (0.72g, 10 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the above described reaction conditions for 24h to afford a mixture of compounds **157** and **158** in the ratio of 33:28 (0.48g, 61%) as an oil.

^{1}H NMR (CCl_4): δ 1.1-1.3 (m, 5H), 1.7 (s, 3H), 1.8-2.0 (m, 3H), 2.5-2.7 (t, 1H, J=6.0 Hz), 4.6 (s, 2H).

IR (neat): υ_{max} 1718, 1360, 1245 cm^{-1}.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.00; H, 8.43.

Found: C, 72.10; H, 8.40.

5,6-Epoxycholestanone (162). Cholesterol (0.4g, 1 mmol), 2-methylpropanal (0.2g, 2 mmol) and cobalt(II) complex **99c** (5 mol%) under the above reaction conditions in 24h afforded **162** (0.27g, 69%).

^{1}H NMR (CCl_4):δ 0.7 (s, 3H), 0.8 (s, 3H), 0.9-1.0 (m, 9H), 1.0-2.0(m, 24H), 2.0-2.6 (m, 5H).

IR (CCl_4):υ_{max} 1715 cm^{-1}.

MS (m/z): 402(M^++1), 401(M^+, 100), 133, 119, 105, 95, 81, 69, 55, 43, 29.

Anal. Calcd. for $C_{27}H_{44}O_2$: C, 80.70; H, 10.47.

Found: C, 80.66; H, 10.49.

Compound 164. α_1-Sitosterol (0.43g, 1 mmol), 2-methylpropanal (0.21g, 3 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the above reaction conditions for 24h to furnish **164** (0.26g, 62%) as solid.

^{1}H NMR(CCl_4): δ 0.6-1.0(m, 18H), 1.0-2.5(m, 28H), 4.8-5.3(m, 2H).

IR(KBr): υ_{max} 1715 cm^{-1}.

Anal. Calcd. for $C_{30}H_{48}O$: C, 84.76; H, 11.30

Found: C, 84.84; H, 11.61.

mp. 154-155° C.

5.12 General Procedure for the Synthesis of 1,2-Diones. Aromatic aldehydes (2.5 mmol), n-butanal (catalytic) and cobalt(II) chloride (5 mol%) were stirred at ambient temperature for 25-30h using calcium chloride guard tube. The solvent was removed in vacuo and the residue was dissolved in diethyl ether and successively washed with saturated $NaHCO_3$ solution (4x20 ml), water (2 x 15 ml) and brine (2 x 20 ml). Drying (Na_2SO_4) and removal of the solvent in vacuo, gave the crude compound which was purified by crystallization.

4,4'-Difluorobenzyl(176). 4-Fluorobenzaldehyde (0.25g, 2 mmol), n-butanal (catalytic amount) and cobalt(II) chloride (5 mol%) under the above reaction conditions for 20h gave **176** (0.2g, 82%) as yellow crystalline solid.

^{1}H NMR (CCl_4): δ 7.5 (d, 4H, J=7 Hz), 8.1 (d, 4H, J=7.0 Hz).

IR (KBr):υ_{max} 1684 cm^{-1}.

mp: 117° C.

4,4'-Dichlorobenzyl (178). 4-Chlorobenzaldehyde (0.28g, 2 mmol) in the presence of n-butanal(catalytic amount) and cobalt(II) chloride (5 mol%) underwent homocoupling to give **178** (0.2g, 70%) as yellow solid.

^{1}H NMR (CCl_4): δ 7.4 (d, 4H, J=7.0 Hz), 7.8 (d, 4H, J=7.0 Hz).

IR (KBr): υ_{max} 1684 cm^{-1}.

MS (m/z): 278(M^+), 241, 57, 45, 29.

mp.:120-121° C.

4,4'-Dibromobenzyl(179). The reaction of 4-bromobenzaldehyde (0.37g,2 mmol) and n-butanal (catalytic amount) in the presence of cobalt(II) chloride (5 mol%) in 35h gave **179** (2g, 57%) as yellow crystalline solid.

^{1}H NMR (DMSO-d_6): δ 7.9 (d, 4H, J=7.0 Hz), 8.2 (d, 4H, J=7.0 Hz).

IR(KBr): υ_{max} 1684 cm^{-1}.

MS(m/z): 367(M^+), 77, 51, 43, 27.

mp.: 178-179°C.

4,4'-Dicyanobenzyl (180). 4-Cyanobenzaldehyde (0.26g, 2 mmol) and n-butanal (catalytic amount) in the presence of cobalt(II) chloride (5 mol%) under the above reaction conditions gave **180** (0.08g, 33%) as yellow crystalline solid. ether .

^{1}H NMR (DMSO-d_6): 7.9 ((d, 4H, J=7.0 Hz), 8.2 (d, 4H, J=7.0 Hz).

IR (KBr): υ_{max}1685 cm^{-1}.

MS (m/z): 238(M^+).

mp.: 170° C.

4,4'-Dimethylbenzyl(181). 4-Methylbenzaldehyde (0.24g,2 mmol), n-butanal (catalytic amount) and cobalt(II) chloride (5 mol%) were subjected to the reaction conditions as described in the general procedure for 25h to afford **181** (0.13g, 57%) as yellow crystalline solid.

^{1}H NMR (CCl_4): δ 1.95 (s, 6H), 7.0 (d, 4H, J=7.0 Hz), 8.0 (d, 4H, J=7.0 Hz).

IR (KBr): υ_{max} 1684 cm^{-1}.

MS(m/z): 57, 45, 29.

mp.: 127-128° C.

Compound 182. 2-Pyridinecarboxaldehyde (0.21g,2 mmol), n-butanal (catalytic) and cobalt(II) chloride (5 mol%) under the above reaction conditions in 35h afforded **182** (0.19g, 92%) as yellow colored solid.

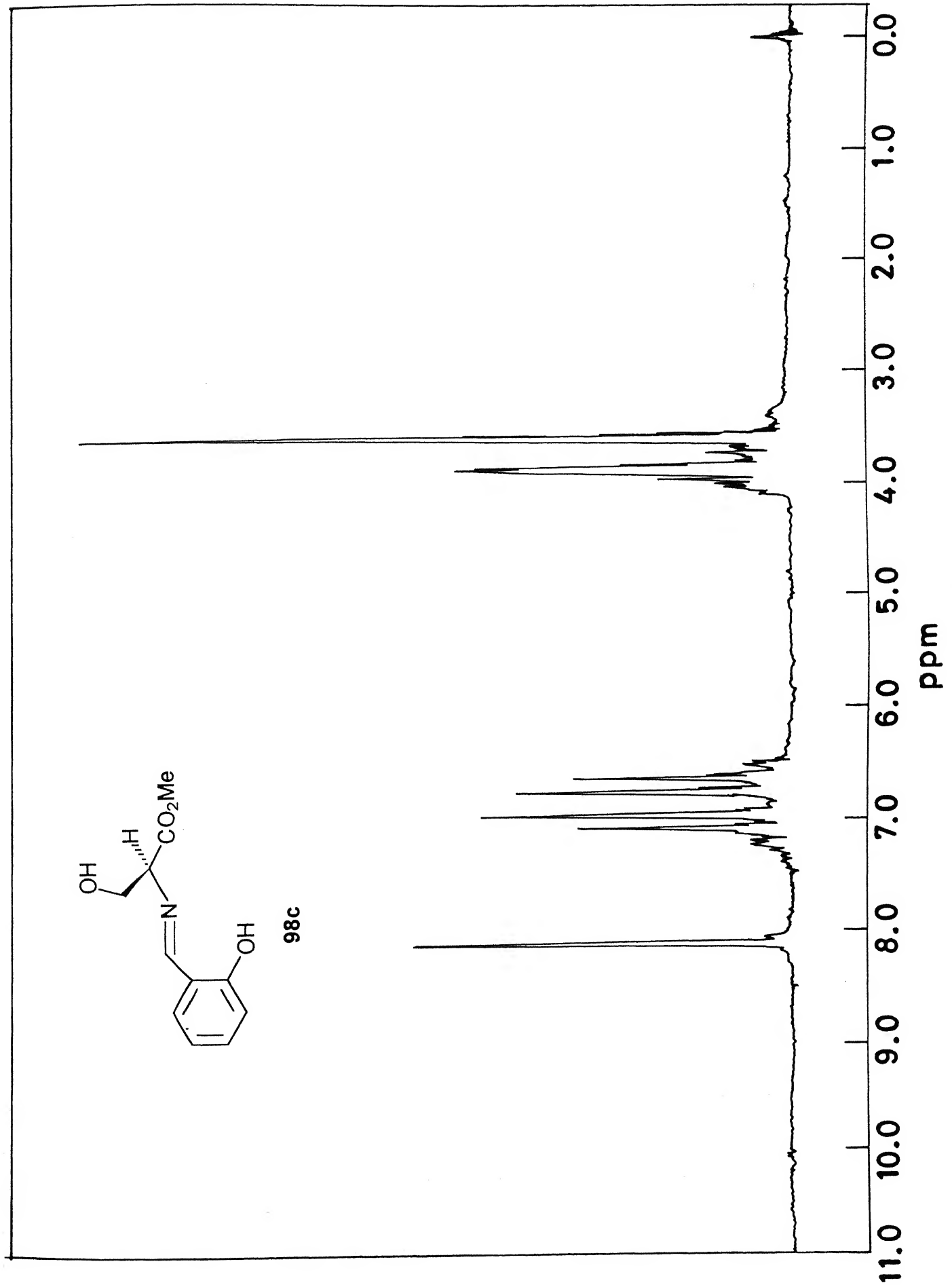
^{1}H NMR (DMSO-d_6): δ 7.1-8.6(m, 8H).

IR (KBr): υ_{max} 1712, 1689 cm^{-1}.

MS (m/z): 214(M^++1), 213(M^+), 78.

mp.: 102-103° C.

5.13General Procedure for the Synthesis of Carboxylic Acids. Benzaldehyde (2.5 mmol), n-butanal (7.5 mmol) and acetic anhydride (7.5 mmol) and cobalt(II) chloride (5 mol%) were stirred at ambient temperature in acetonitrile (30 ml) using calcium chloride guard tube for 30-35h. Usual workup and crystalization afforded the acids in good yields.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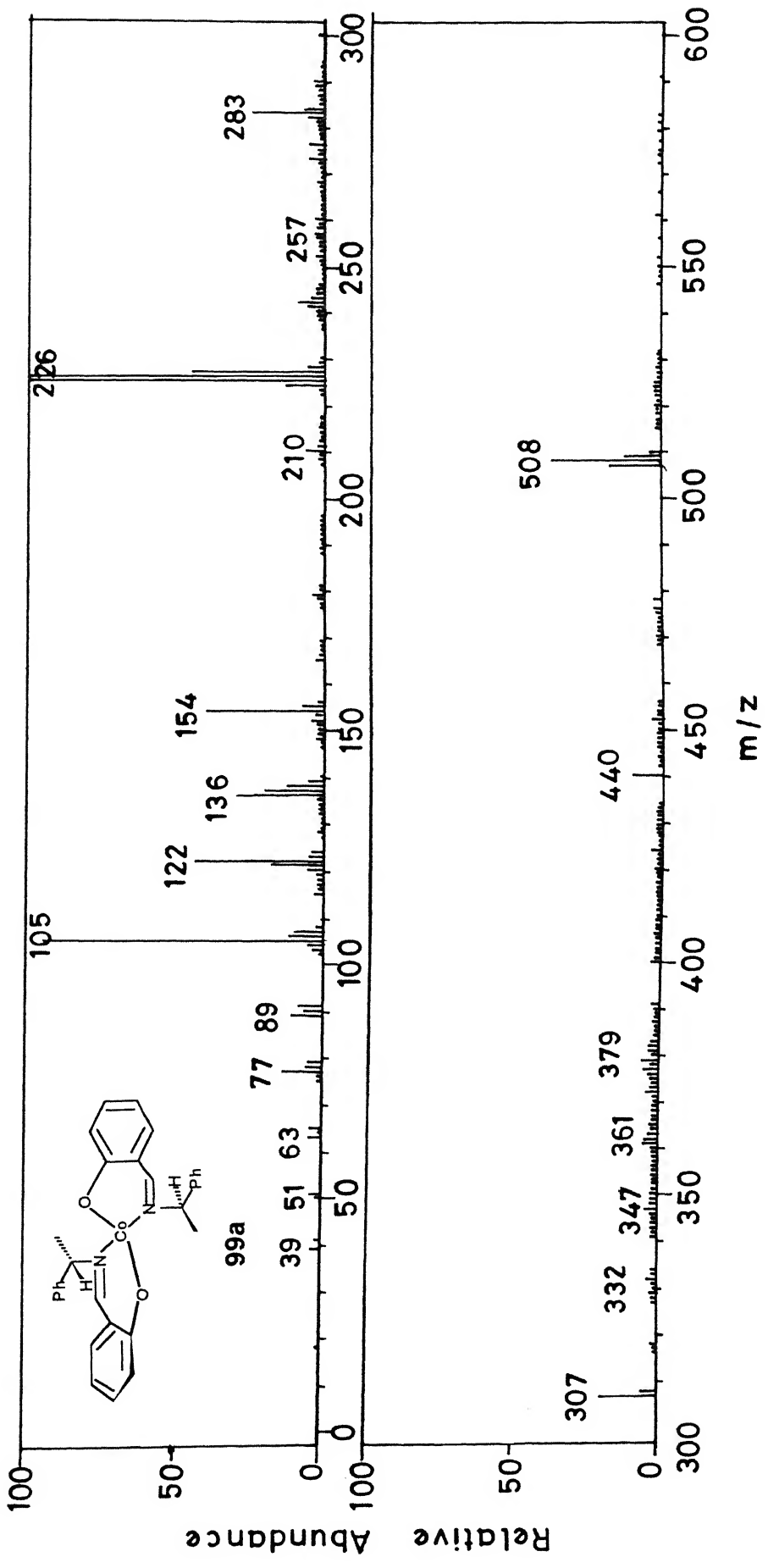
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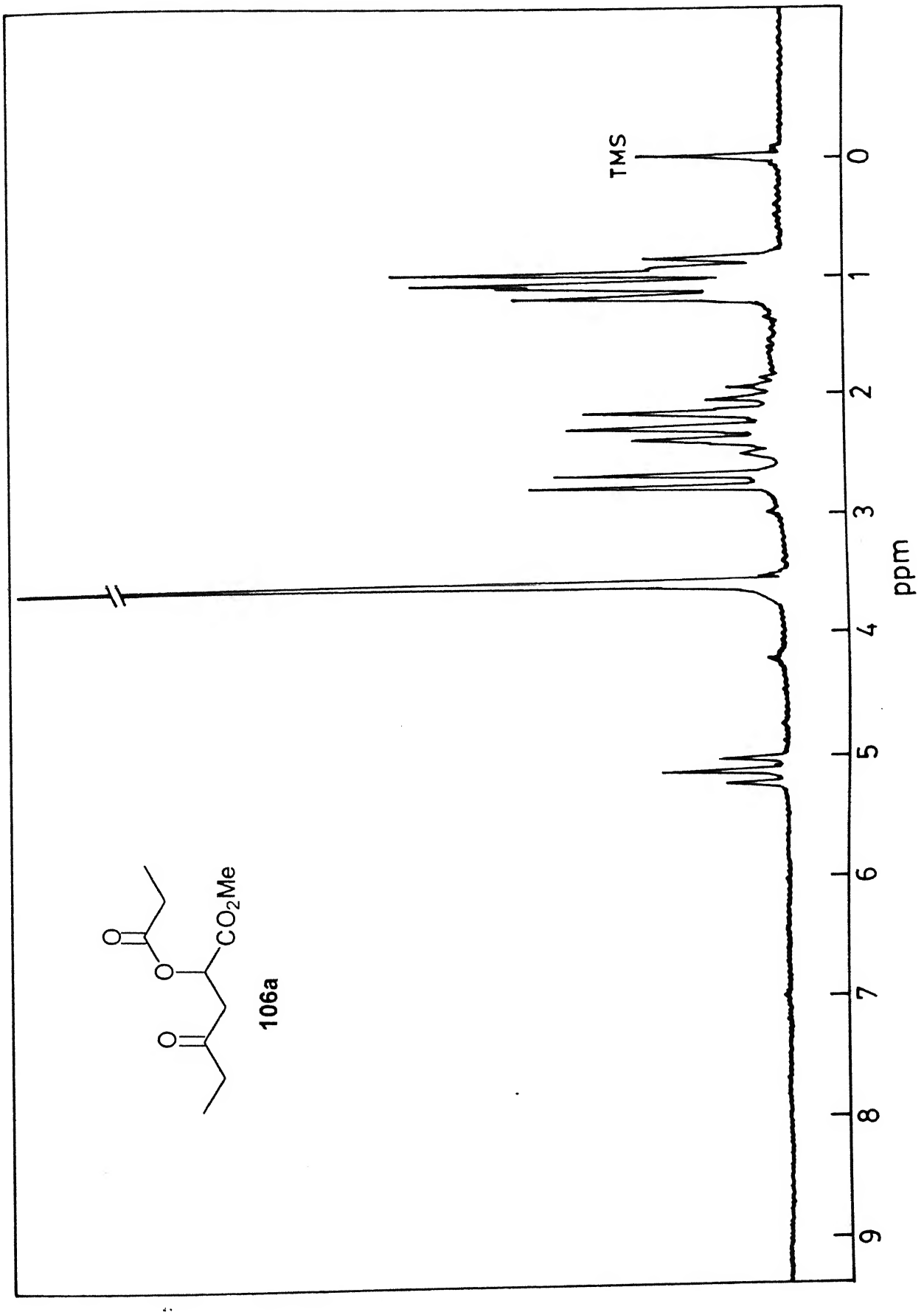

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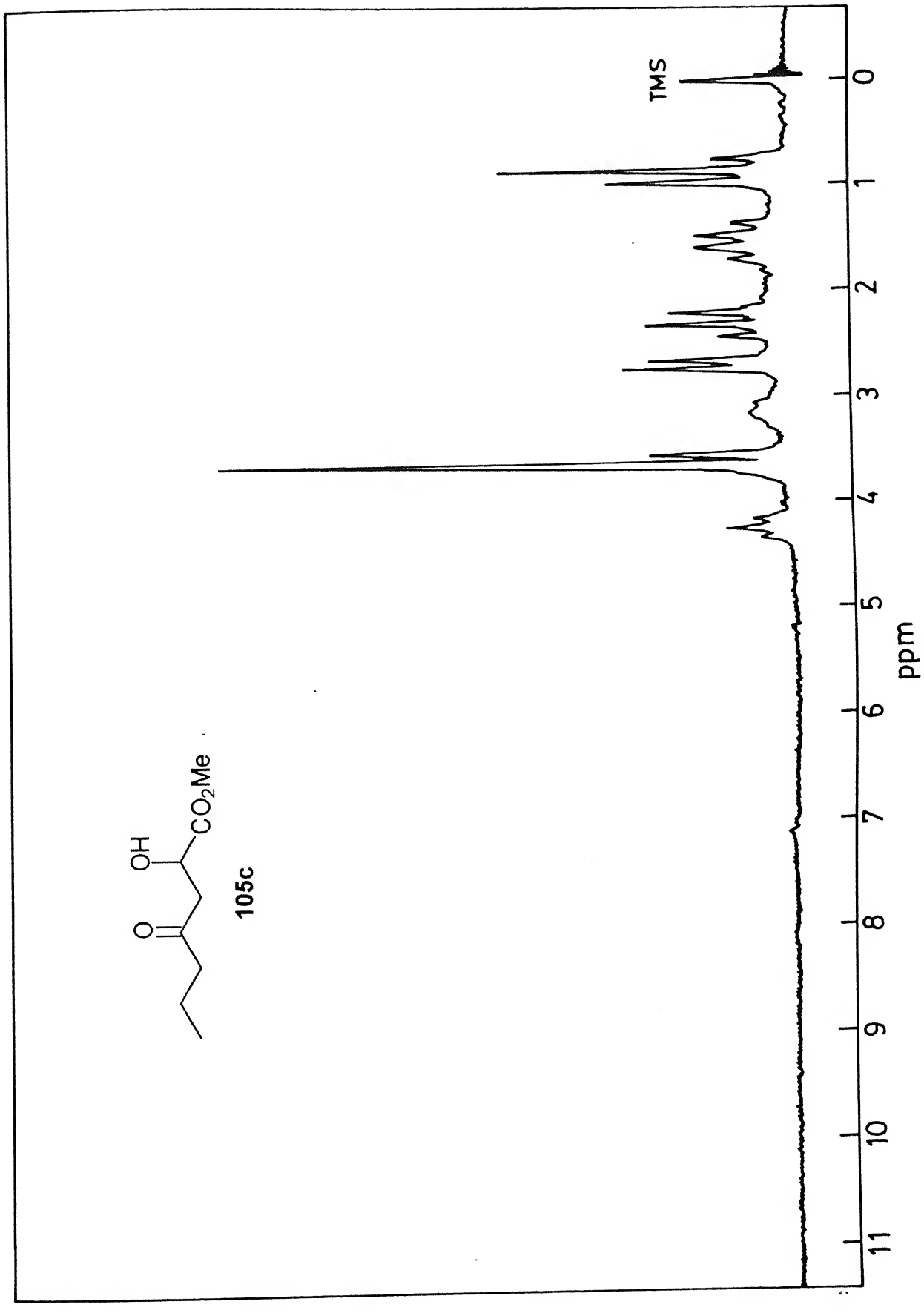
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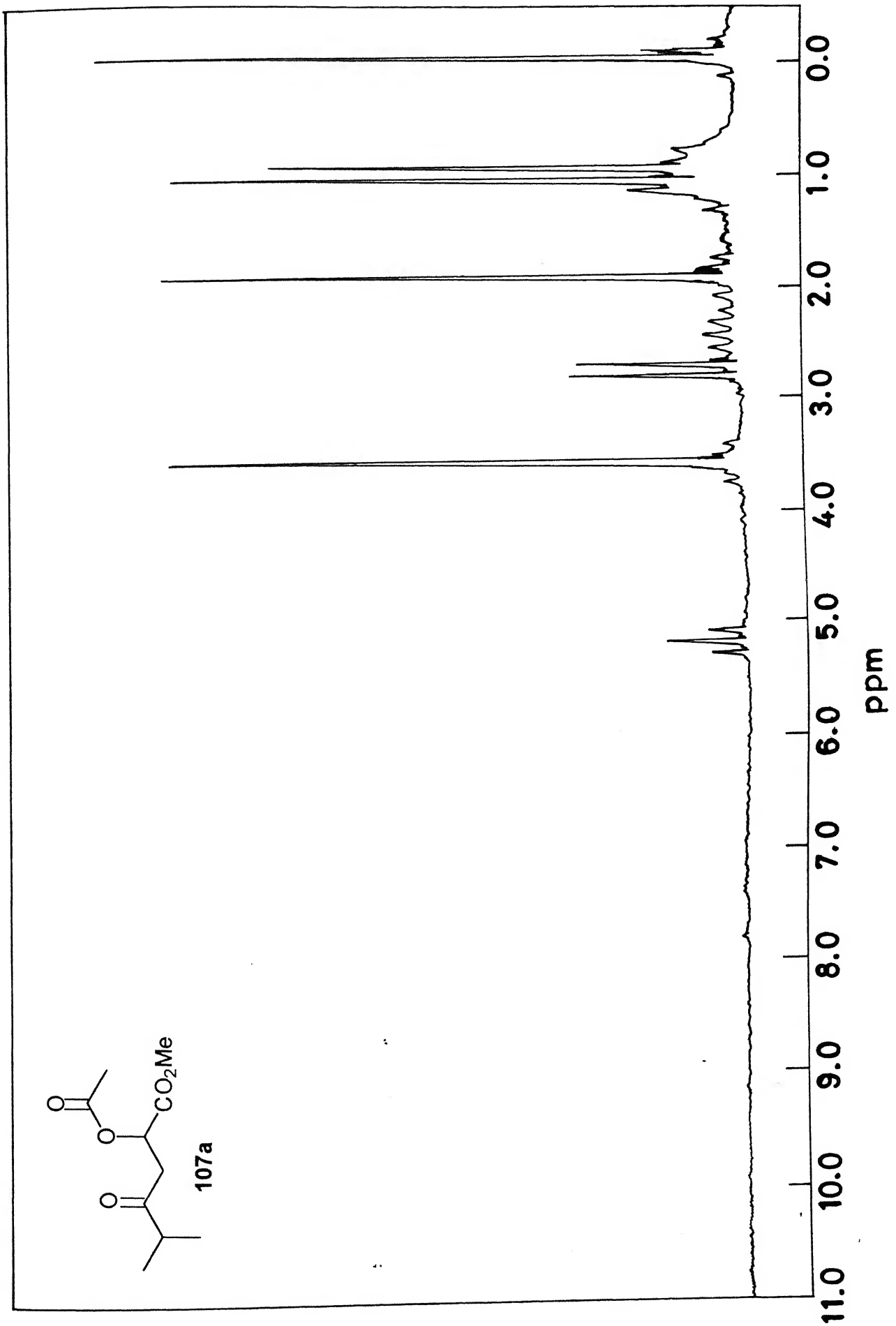
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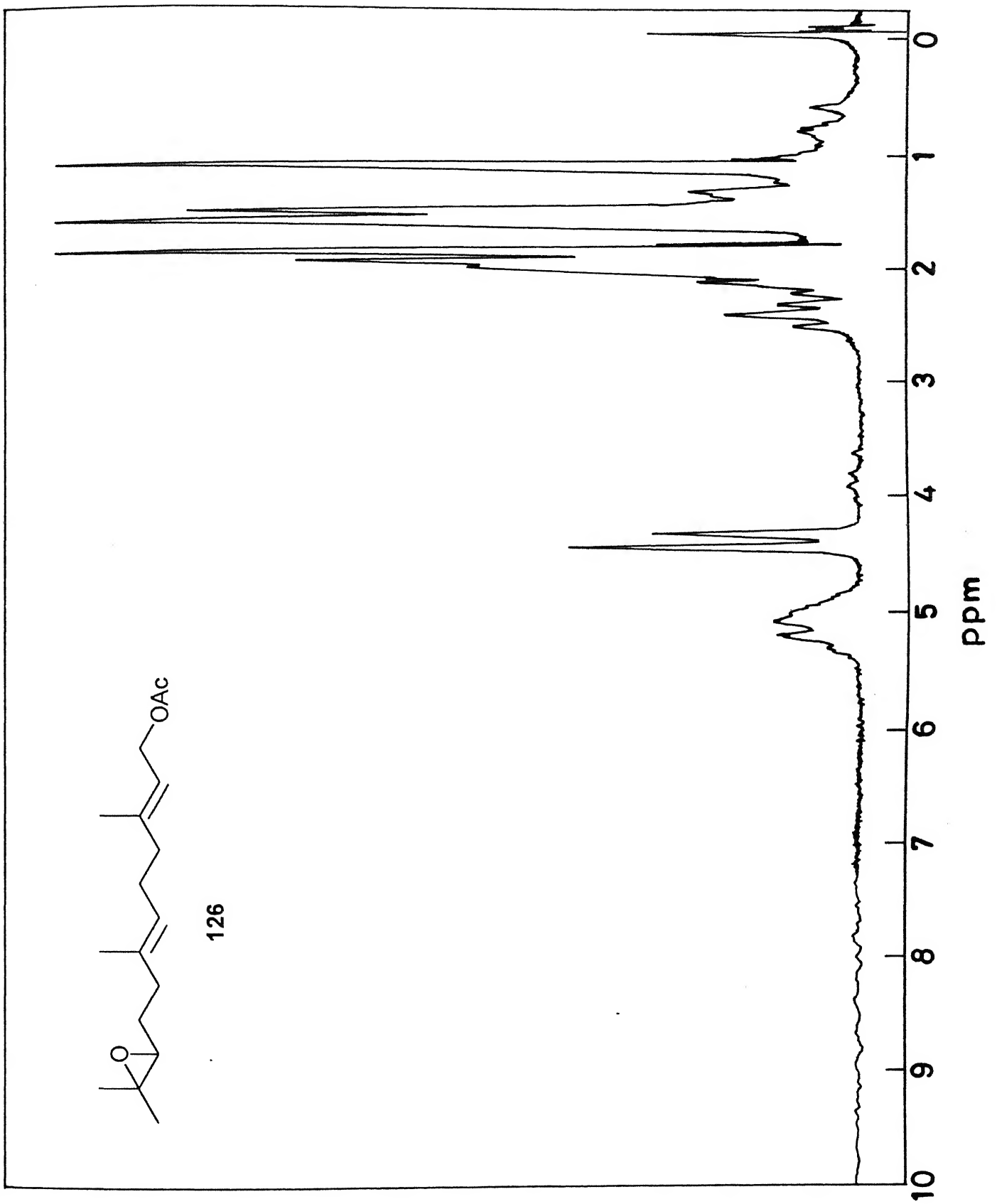
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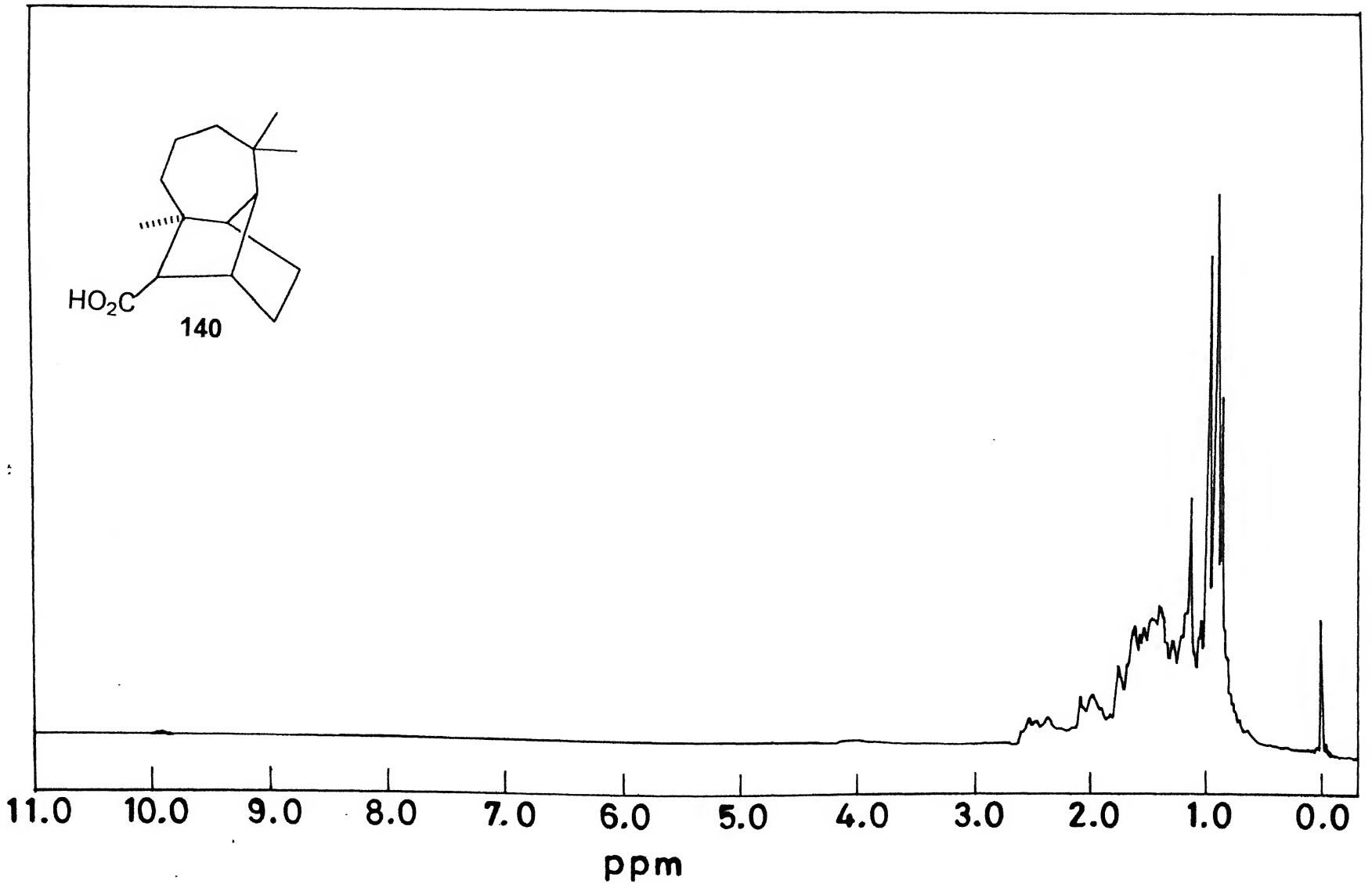
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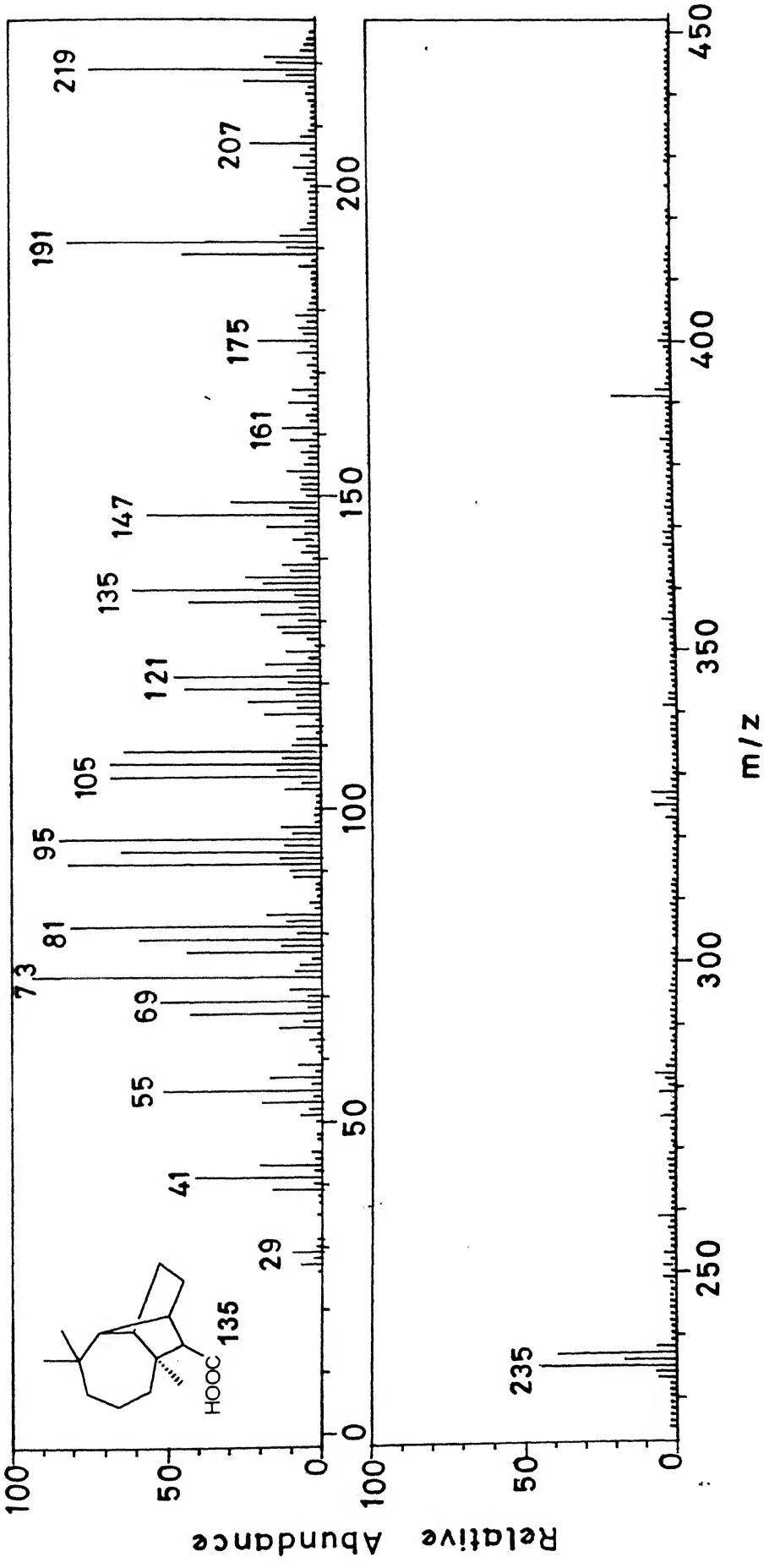
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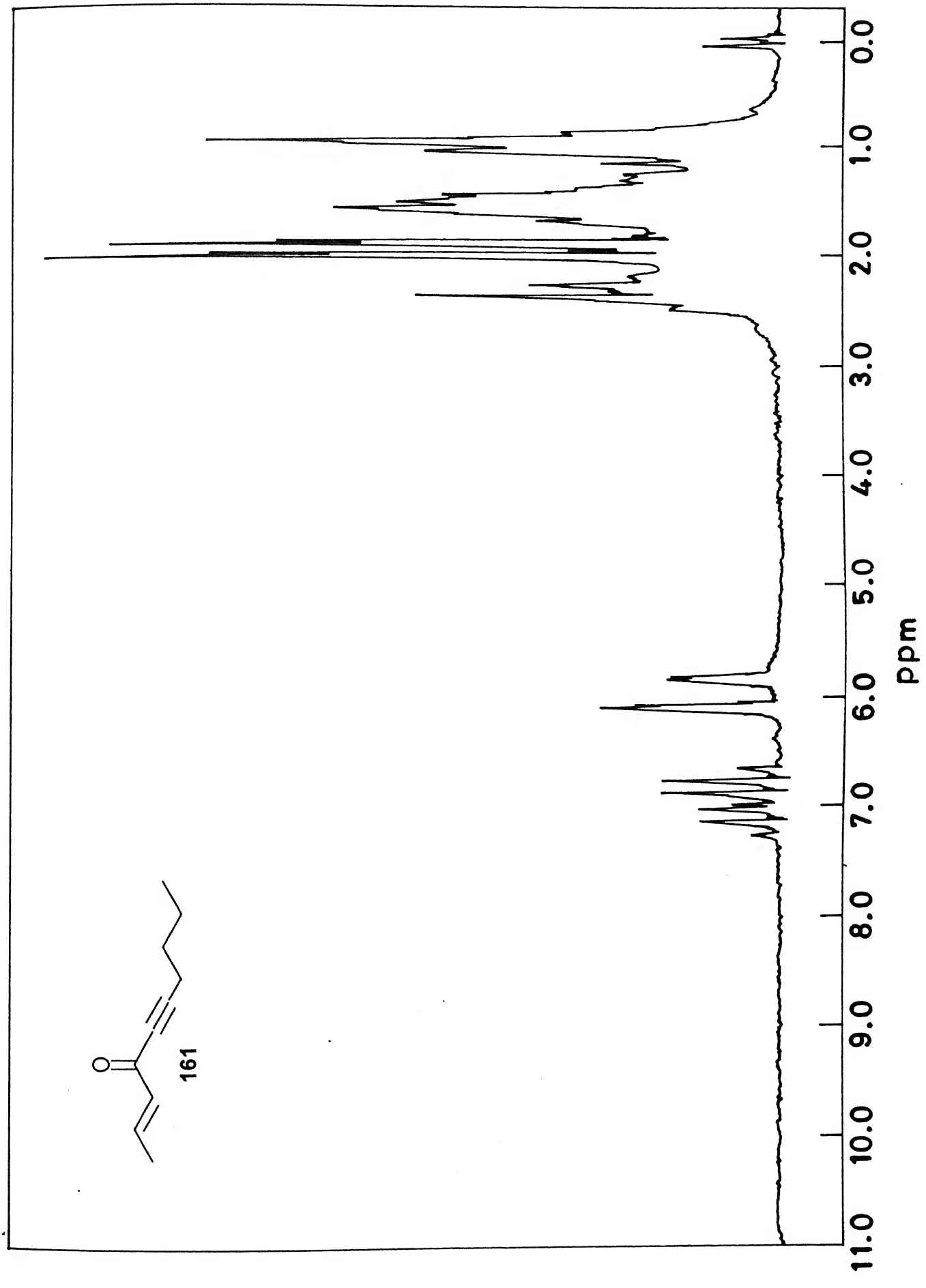
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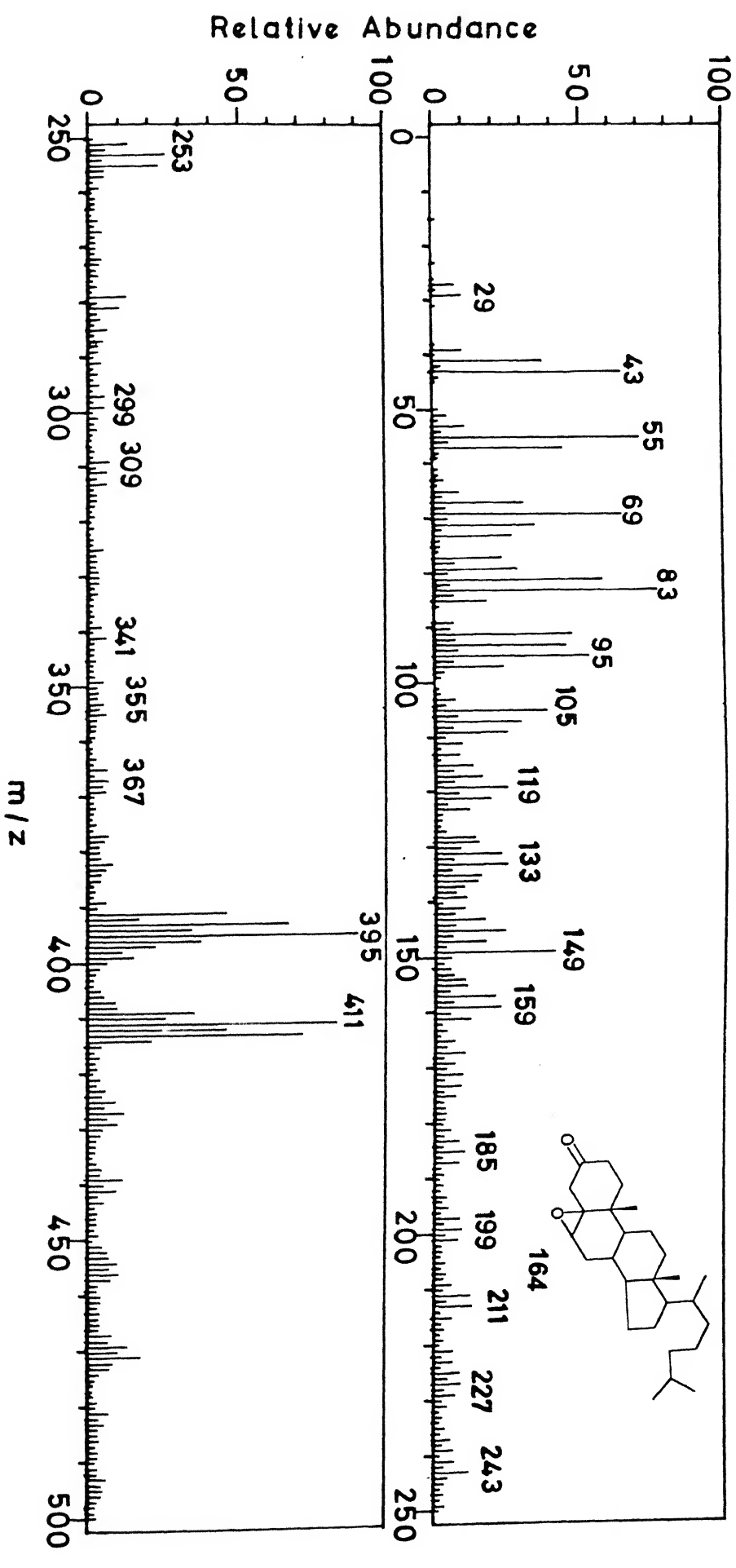
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Part Two

Cobalt Catalyzed Generation and Reactivity of 1,3-Dicarbonyl Radical from β-Ketoesters in the Presence of Dioxygen

Cobalt(II) Schiff Base Complex Catalysed Reaction of 1,3-Dicarbonyl Compounds with Various Organic Substrates in the Presence of Dioxygen

6.1 Introduction

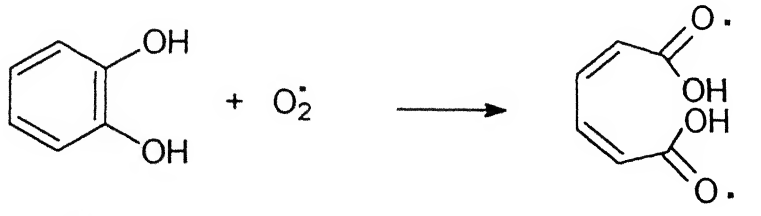
Oxygen, the most abundant element, in its free and combined states, constitutes 46.6% of the earth crust. Combining dioxygen with hydrocarbons is a rewarding goal as it leads to valuable oxygenated products such as alcohols, ketones, epoxides etc.

Biological Aspects

Dioxygen plays a central role in living cells. It can either be transported by respiratory pigments and released at active sites, or activated in enzymatic systems called oxygenases. At physiological temperature these oxygenases play a crucial role in many fundamental biological processes such as degradation of natural products in the biosphere, biosynthesis and metabolism of amino acids, hormones, drugs, etc. A wide variety of enzymic oxygenases has been identified and isolated from microorganisms, plants and animals. The main relevant characteristic properties of oxygenases are that they mostly involve transition metals as active center[1]. Transition metals having multiple spin and oxidation states can readily interact with dioxygen, even to the extent of forming isolatable oxygen adducts[2-13]. In these associations, the metal acts as a reducing agent and can also polarize the dioxygen bond, facilitating its cleavage. It can also

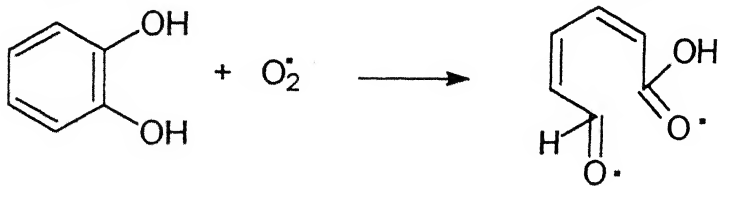
simultaneously bind dioxygen and the substrate, and then create the favorable entropic conditions for a selective oxidation to occur. Oxygenases can be conveniently classified into two main families.

(1) *Dioxygenases* catalyze the incorporation of both atoms of dioxygen into the substrate. Microbial *pyrocatechol dioxygenases* contain non-heme iron as the sole cofactor and catalyze the oxidative cleavage of pyrocatechol **192** to cis,cis-muconic acid **193** (intradiol; Eq. 16) or to α-hydroxymuconic *ξ-semialdehyde **194*** (extradiol; Eq. 17)[14-16]. On the other hand, *tryptophan 2,3-dioxygenase* contains both ferriprotoporphyrin IX and cuprous ion as the active site and catalyzes the oxidative cleavage of L-tryptophan **195** to formylkynurenine **196** (Eq. 18)[17].



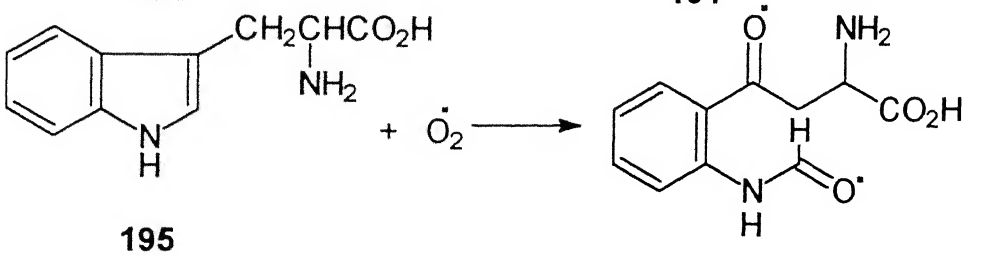
(Eq. 16)

192 **193**



(Eq. 17)

192 **194**



(Eq. 18)

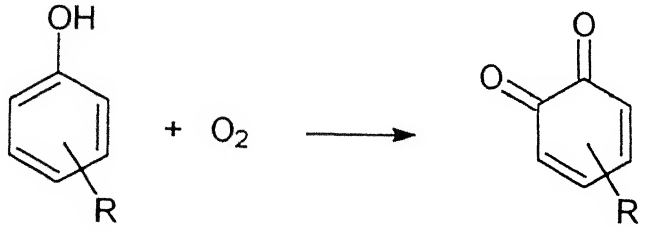
195 **196**

(2) *Monooxygenases* catalyze the incorporation of only one atom of molecular oxygen into the substrate, while the other one is reduced to water. In *internal monooxygenases* the hydrogen donor is the substrate itself (Eq. 19), while *external monooxygenases* require a hydrogen donor

cosubstrate DH_2 (Eq. 20), such as $NADPH_2$ or $NADH_2$. Tyrosinase is one example of an internal monooxygenase; it contains copper as the active metal and transforms phenols **197** into o-quinones **198** (Eq. 21)[18,19]. External monooxygenases containing cytochrome P-450 as an active center have been extensively studied in recent years[20-24]. Cytochrome P-450 molecules comprise hemoproteins containing ferriprotoporphyrin IX bonded to a polypeptide chain by a cysteinate sulfide atom acting as a strongly donating axial ligand. They have been isolated from numerous bacteria, adrenal mitochondria and mammalian liver microsomes.

$$SH_2 + O_2 \longrightarrow SO + H_2O \qquad \text{(Eq. 19)}$$

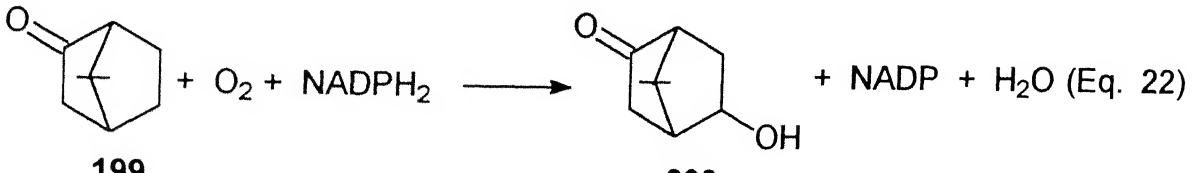
$$S + DH_2 + O_2 \longrightarrow SO + D + H_2O \qquad \text{(Eq. 20)}$$



(Eq. 21)

197 **198**

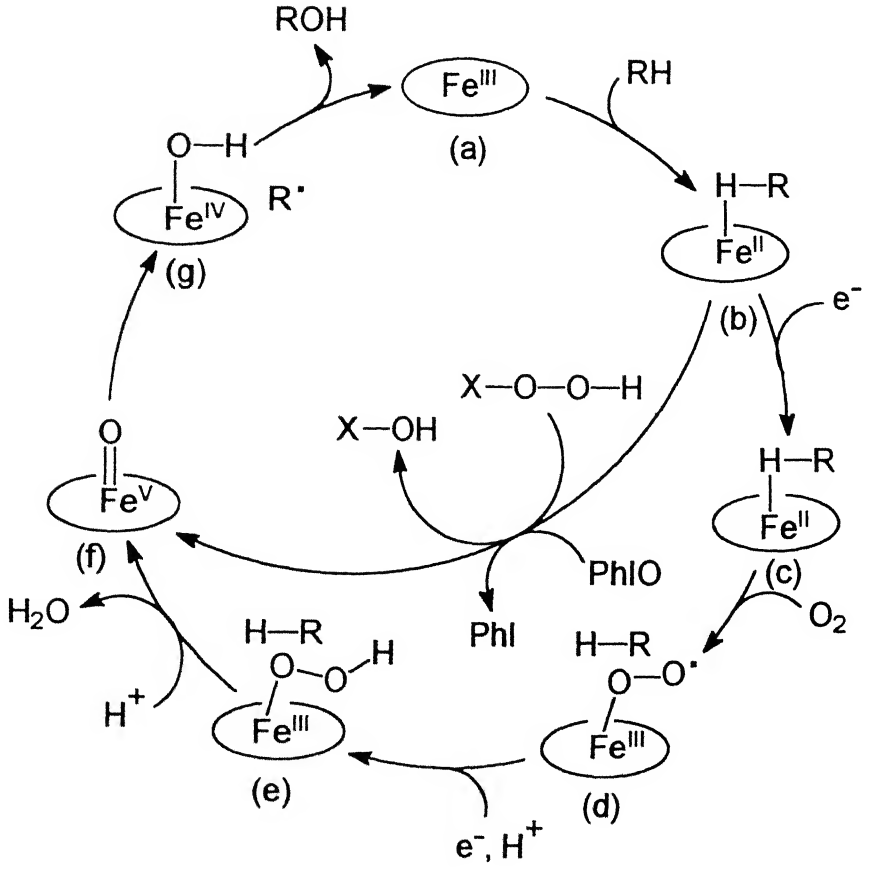
The camphor 5-oxygenase of *Pseudomonas putida*, which has been isolated in crystalline form, catalyzes the hydroxylation of camphor (Eq. 22)[20].



199 **200**

In mammalian liver microsomes, cytochrome P-450 is not specific and catalyzes a wide variety of oxidative transformations, such as: (i) aliphatic C-H hydroxylation occurring at the most nucleophilic C-H bonds (tertiary> secondary>primary); (ii) aromatic hydroxylation at the most nucleophilic positions with a characteristic intramolecular migration and retention of substituents of the aromatic ring, called an NIH shift[25], which indicates the intermediate formation of arene oxides; (iii) epoxidation of alkenes; and (iv) dealkylation (O, N, S) or

oxidation (N, S) of heteroatoms. In mammalian liver these processes are of considerable importance in the elimination of xenobiotics and the metabolism of drugs, and also in the transformation of innocuous molecules into toxic or carcinogenic substances[26-28].



Scheme 42

It is now generally understood that the mechanism of hydroxylation by cytochrome P-450 proceeds by two successive one electron reduction steps of the heme center, transforming dioxygen into a peroxide species bonded to iron (Scheme 42)[24,29]. Well-defined steps (a)-(g) involve: (i) the formation of a high-spin Fe(III)-enzyme-substrate complex (b); (ii) one-electron

reduction of (b) to a high-spin ferrocytochrome (c); (iii) addition of dioxygen to form a superoxo-Fe(III) complex (d); and (iv) one-electron reduction of the superoxo complex to a peroxide complex (e).

The mechanism of oxygen transfer from the peroxide (e) to the substrate still remains a matter of controversy. Current opinions favor the formation of a high-valent FeO(III) (or Fe(V)=O or Fe(IV)-O·) (f) active species, which acts as a homolytic hydrogen abstractor from the substrate[29,30]. An alternative mechanism considers the Fe(III)-peroxide complex as the actual hydroxylating reagent[12], by analogy with the reactivity of vanadium(V)-peroxo[31] and -alkylperoxo complexes[32] and that of chromium(VI)-peroxo complexes.[33,34]

Industrial Aspects

Millions of tons of oxygenated compounds are annually produced in the world and find applications in all areas of the chemical industry[35-46]. The main industrial oxygenated products obtained by catalytic oxidation. Most of these processes use dioxygen or air as the oxidant and operate under homogeneous or heterogeneous conditions (Table 23).

The liquid-phase oxidation of hydrocarbons represents the largest scale application of homogeneous catalysis. Liquid-phase process technology enables better control of reaction conditions and conversions, and more convenient heat removal from these highly exothermic oxidations.

Homolytic liquid-phase processes are generally well suited to the synthesis of carboxylic

Table 23. Main Industrial Catalytic Oxidation Processes

Product	Substrate	Oxygen source	World capacities(Mty^{-1})	Reaction conditons	Chemical characteristics	Process	Main applications
Formaldehyde	Methanol	O_2	5	350°C, 1 bar, $[Fe(MoO_4)_3]$	Heterogeneous, heterolytic	Perstop-Reichhold, Hiaq-Lurgi, Lummus Montedison, SBA IFP-CDF	Resins, polyols conservatipn
Ethylene oxide	Ethylene	O_2	7.5	270°C, 10-30 bar, [Ar]	Heterogeneous, heterolytic	UCC, Shell, CI Scientific Design	Ethylene glycol, polyesters
Acrylic acid	propene	O_2	1.3	$C_3 \longrightarrow$ acrolein 350°C $[Bi_2O_3MoO_3]n$, acrolein $\longrightarrow$ acrylic acid: 250°C, [Mo/V]	Heterogeneous, heterolytic	UCC, Autochem, Shell Sohio, Nippon, Shokubai	Polymers
Benzoic acid	Toluene	O_2	0.5	120°C, 3 bar [Co/Br], AcOH	Homogeneous, homolytic	Dow, Amoco	Phenol
Phthalic anhydride	Naphthalene	O_2	2	400°C, 3 bar [V/Mo], AcOH	Heterogeneous, heterolytic	Chemisches, Cyanamid, ICI, Rh-Poulenc	Plasticizers

acids, *viz.* acetic, benzoic or terephthalic acids which are resistant to further oxidation. These processes operate at high temperature (150-250°C) and generally use soluble cobalt or manganese salts as the main catalyst components. High conversions and selectivities are usually obtained with methyl-substituted aromatic hydrocarbons such as toluene and xylenes[47,48]. The cobalt-catalyzed oxidation of cyclohexane by air to a cyclohexanol-cyclohexanone mixture is a very important industrial process since these products are intermediates in the manufacture of adipic acid and caprolactam. However, the conversion is limited to *ca.* 10% in order to prevent consecutive oxidations, with roughly 70% selectivity[49].

Heterolytic liquid-phase oxidation processes are more recent than homolytic ones. The two major applications are the Wacker process for oxidation of ethylene to acetaldehyde by air, catalyzed by $PdCl_2$-$CuCl_2$ systems,[50] and the Arco oxirane[51] or Shell process[52] for epoxidation of propylene by t-butyl or ethylbenzene hydroperoxide catalyzed by molybdenum or titanium complexes. These heterolytic reactions require less drastic conditions than the homolytic ones and are much more selective.

Heterogeneous oxidative processes operate at high temperatures (250-450° C) and are useful for the synthesis of acrolein and acrylic acid from propylene over bismuth molybdate catalysts, the synthesis of maleic and phthalic anhydride from the oxidation of benzene (or C_4 compounds) and naphthalene (or o-xylene) respectively over vanadium oxide[53], and the synthesis of ethylene oxide from ethylene over silver catalysts[54].

Owing to space limitations, only the most representative examples of oxidations mediated by transition metal complexes in the presence of dioxygen will be discussed in this introduction.

introduction.

6.1.1 Rhodium

Read and coworkers have found that rhodium complexes such as $RhCl(PPh_3)_3$ were able to promote the oxygenation of terminal alkenes to methyl ketones and PPh_3 to Ph_3PO using conditions under which a Wacker-type oxidation (hydroxymetalation of the coordinated alkenes by water) was disfavoured (Eq. 23)[55].

$$RCH{=}CH_2 + PPh_3 + O_2 \xrightarrow[C_6H_6]{RhCl(PPh_3)_3} R{-}\overset{\overset{O}{\|}}{C}{-}Me + Ph_3PO \qquad \text{Eq. 23}$$

In this reaction, one oxygen atom of the dioxygen molecule is incorporated into the alkene, while the phosphine acts as a coreducing agent with the second oxygen atom to produce phosphine oxide. In the absence of phosphines and under more forced conditions, the use of Rh^I complexes as catalysts for the autoxidation of alkenes result into the formation of the expected ketone together with allylic or cleaved oxygenated products, presumably coming from parallel radical chain reactions[56-60].

The use of rhodium trichloride associated with copper(II) perchlorate or nitrate in an alcoholic solvent resulted into a major improvement in the catalytic oxidation of terminal alkenes by dioxygen at room temperature, without the need for a coreducing agent (Eq. 24)[61].

$$2RCH_2{=}CH_2 + O_2 \xrightarrow[EtOH,\ 20\text{-}80^0\ C]{RhCl_3 + Cu(ClO_4)_2} 2R{-}\overset{\overset{O}{\|}}{C}{-}Me \qquad \text{Eq. 24}$$

$$\geq 98\%$$

In this reaction, both oxygen atoms are incorporated into two moles of alkene to give two moles of ketone with selectivity, based on consumed alkene and molecular oxygen, of upto

98%. The characteristic of the reactions are different from conventional Wacker chemistry.

(1) In contrast to the corresponding palladium system, water is not involved as the oxygen source. In fact it is an inhibitor, and the presence of a dehydrating agent such as 2,2-dimethoxy-propene speeds up the reaction.

(2) Although the alcohol solvent does not act as a coreducing agent, it is necessary for the reaction and probably intervenes in the formation of active species[61,62].

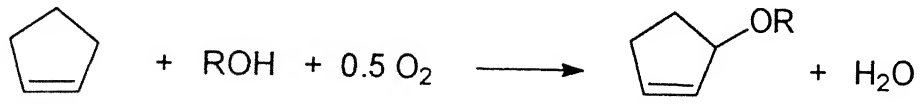
(3) The presence of copper(II) salts, in the optimum ratio Cu:Rh=1 or 2, considerably increase the rate and the selectivity of the reaction. Rhodium perchlorate alone acts as a catalyst, but cooxidises the solvent alcohol to a carbonyl compound. With Cu:Rh=1, 85% of the copper precipitates from the reaction mixture as CuCl.

(4) The presence of chloride anions in an optimum ratio Cl:Rh=2 or 3 and an acidic medium (H^+:Rh=3) are necessary for the reaction[61-63].

(5) The nature of the oxidation products is traceable to the nature of the rhodium-alkene interaction. Terminal alkenes and cyclic alkenes, which form π-complexes of rhodium(I) eg.$[RhCl(alkene)_2]_2$, are selectively converted to methylketones, whereas alkenes which form π-allylic complexes or rhodium(III) (eg. cyclopentene) give alkenyl ethers via oxidative substitutions of the alkene by the solvent alcohol (Eq. 25)[61].

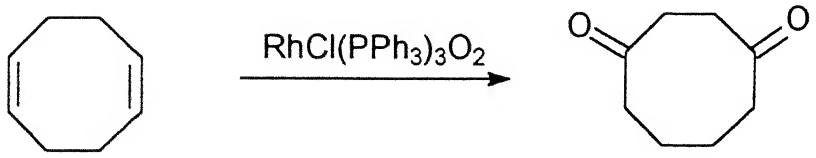
(6) The $RhCl_3$-$Cu(ClO_4)_2$ catalyzed oxidation of 1-hexene is first order dependent on

rhodium and alkene concentration, and independent of dioxygen pressure. In fact, higher molecular oxygen partial pressure inhibits the reaction. Strongly complexing alkenes, eg. cyclooctene, were found to be less reactive than terminal ones. Further, the reaction is strongly inhibited by ligands eg. PPh_3, or strongly complexing dialkenes eg. 1,5-cyclooctadiene.



201 **202** Eq. 25

As recently reported, rhodium-dioxygen complexes such as $RhCl(O_2)(PPh_3)_2$ can transfer both dioxygen atoms to one mole of coordinated 1,5-cyclooctadiene **203** to give cyclooctane-1,4-dione **204**, without the intermediate formation of monoketone (Eq. 26). In the presence of excess of PPh_3, the reaction becomes slightly catalytic[64].



203 **204** Eq. 26

6.1.2 Palladium

6.1.2.1 Oxidation of Alkenes to carbonyl compounds

The oxidation of ethylene to acetaldehyde by palladium(II) salts in an aqueous solution was discovered by Phillips in 1894[65], and was developed into a commercial process about 60 years later by Smit and coworkers at Wacker Chemie[66,67]. These researchers succeeded in transforming this stoichiometric oxidation by a precious metal (Eq. 27) into a catalytic reaction

through the reoxidation of the resulting Pd^0 by dioxygen in the presence of copper salts (Eq. 28 and 29).

$$CH_2=CH_2 + PdCl_2 + H_2O \longrightarrow MeCHO + Pd^0 + 2HCl \quad \text{Eq. 27}$$

$$Pd^0 + 2CuCl_2 \longrightarrow PdCl_2 + Cu_2Cl_2 \quad \text{Eq. 28}$$

$$Cu_2Cl_2 + 2HCl + 0.5\,O_2 \longrightarrow 2CuCl_2 + H_2O \quad \text{Eq. 29}$$

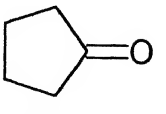
A similar single or two-stage process has been developed for the manufacture of acetone from propene (110-120°C, 10 atm, $PdCl_2$-$CuCl_2$-HCl catalyst) but on a smaller scale (80,000 t/year) than for acetaldehyde (2,500,000 t/year)[68].

Higher alkenes can also be converted to methyl ketone with the Wacker catalyst, but the rates and selectivities are lower. Improved procedures use basic[69,70] or alcoholic solvents[71]. Tsuji and coworkers used the $PdCl_2$/CuCl catalyst in dimethyl formamide for the synthesis of a variety of natural products and fine chemicals[72]. Only terminal alkenes are converted to ketones under these conditions, even when the substrate contains other functional groups[73].

The Wacker $PdCl_2$-$CuCl_2$ catalyst is a highly corrosive one, and its use requires special vessels and apparatus, such as titanium or tantalum alloys. Heteropoly acids have been used as alternative noncorrosive reoxidants of palladium for a variety of organic transformations[74], for example in eq. 30[75].

201

$$+ 0.5\,O_2 \xrightarrow{PdSO_4 / H_3PMo_6W_6O_{40}}$$



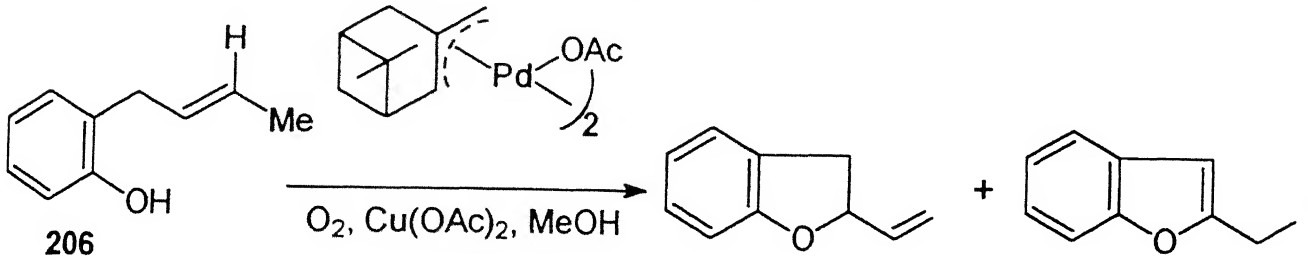
205

100%

Eq. 30

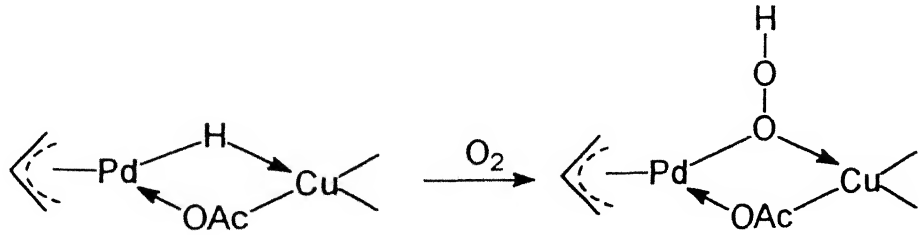
Good yields of carbonyl compounds have also been obtained from the vapor-phase oxidation of alkenes by steam and air over palladium catalysts supported on charcoal[76]. In this case, no copper cocatalyst is needed, presumably because palladium(II) is not reduced to palladium(O), but remains in the form of a stabilized palladium(II) hydride which can react with molecular oxygen to give the hydroperoxidic species.

In fact, the role of copper and oxygen in the Wacker process is certainly more complicated and could be similar to that previously discussed for the rhodium/copper-catalyzed ketonization of terminal alkenes. Hosokawa and coworkers have recently studied the Wacker-type asymmetric intramolecular oxidative cyclization of trans-2-(2-butenyl)phenol by dioxygen in the presence of (+)-(3,2,10-η-pinene)palladium(II) acetate and copper(II) acetate (Eq. 31)[77]. It has



206 **207**(70) **208**(12) Eq. 31

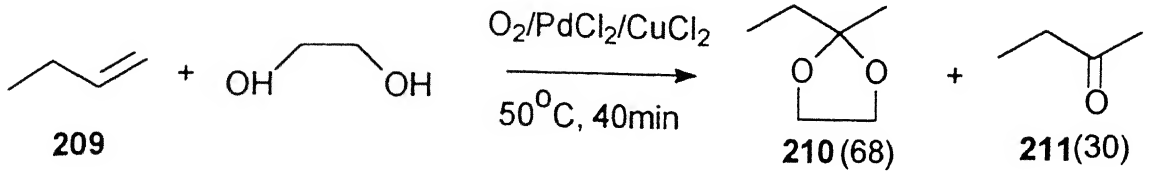
been shown that the chiral pinanyl ligand is retained by palladium throughout the reaction, and therefore it is suggested that the active catalyst consists of copper and palladium linked by an acetate bridge. The role of copper would be to act as an oxygen carrier capable of rapidly reoxidising palladium hydride into a hydroperoxide species (Eq. 32)[77]



Eq. 32

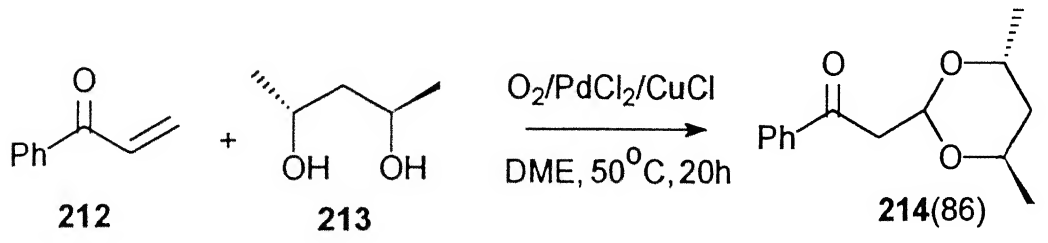
Acetalization of alkenes can be achieved in good yields when the oxidation is carried out in the presence of alcohols or diols. Acetalization of terminal alkenes such as 1-butene **209**

occurs preferentially at the 2-position in the presence of $PdCl_2$-$CuCl_2$ (Eq. 33)[78], whereas



209 **210** (68) **211**(30) Eq. 33

terminal alkenes **212** bearing electron-withdrawing substituents are acetalized at the terminal position in the presence of $PdCl_2$-CuCl in 1,2-dimethoxyethane (Eq. 34)[79].



212 **213** **214**(86) Eq. 34

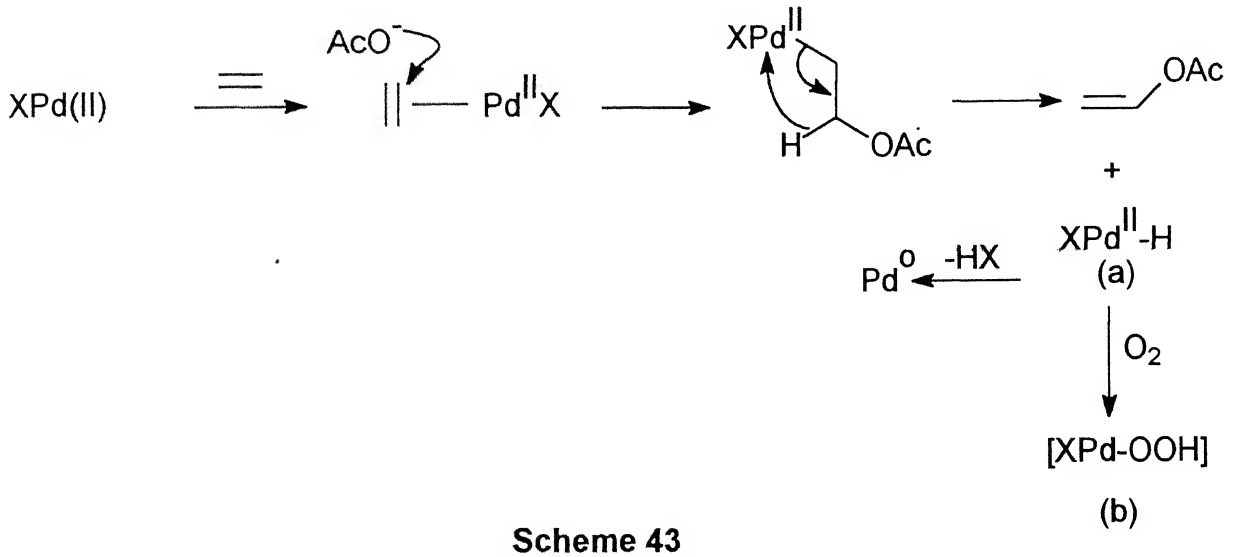
6.1.2.2 Acetoxylation of Alkenes and Dienes

Vinyl acetate from ethylene

Vinyl acetate is an extremely important petrochemical product which is used for the synthesis of polymers such as poly(vinyl acetate) and poly(vinyl alcohol).

The vinyl acetate process exists in both homogeneous and heterogeneous versions. The liquid-phase process developed by ICI is essentially a Wacker reaction performed in acetic acid: ethylene, dioxygen and acetic acid are reacted at 110° in the presence of palladium(II) chloride, copper(II) acetate and hydrochloric acid. Overall yields are greater than 90%. Acetaldehyde is formed as coproduct in the reaction, owing to the presence of water, and is oxidized to acetic acid which is used in the process. However, this process encountered severe corrosion problems and was abandoned[46].

The gas-phase process, successfully commercialized independently by Bayer and USI[80] involves passing a mixture of ethylene, acetic acid and oxygen over a supported palladium catalyst contained in a multitubular reactor at 150° C and about 5-10 atm pressure. The overall yield in vinyl acetate is about 92%, and the major by-product is carbon dioxide. The catalyst consists of a palladium salt (eg. Na_2PdCl_4) deposited on silica (or alumina) in the presence of a cocatalyst (eg. $HAuCl_4$) reduced and impregnated with potassium acetate before use[67,81].

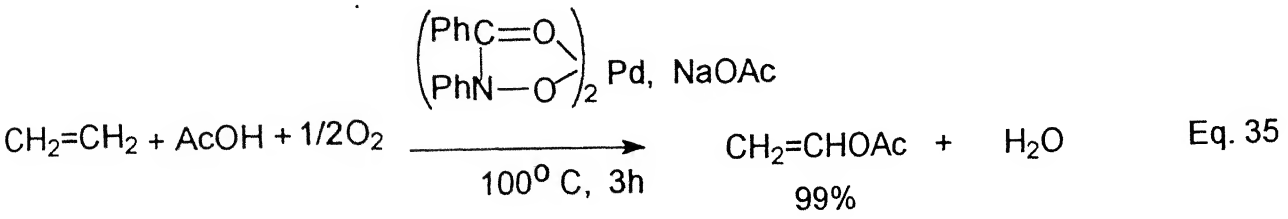


Scheme 43

A widely accepted mechanism for acetoxylation of ethylene is shown in scheme 43 and consists of the nucleophilic attack of the acetate anion on the coordinated ethylene, followed by acetoxypalladation and β-hydride elimination, giving vinyl acetate and palladium hydride[82].

It should be noted that heterogeneous palladium acetoxylation catalysts do not contain copper cooxidants, presumably because the support stabilizes the resulting palladium(II) hydride and prevents the formation of metallic palladium. The stabilized palladium hydride (a) may react with dioxygen to give the hydroperoxide (b), which is probably an important intermediate for the regeneration of the initial Palladium(II) catalyst (Scheme 43).

Such a stabilization of the palladium catalyst can also be achieved in homogeneous liquid phase by the use of appropriate ligands. Thus, it has recently been shown that palladium(II) hydroxymates are effective catalysts for the acetoxylation of ethylene with higher selectivity and a high turnover($\geq$ 200) (Eq. 35), whereas $Pd(OAc)_2$ rapidly becomes deactivated and precipitates in the form of metallic palladium[83]. It is probable that the bidentate hydroxymate ligand stabilizes the hydride species (Pd-H) and prevents palladium from precipitating.



Eq. 35

6.1.2.3 Oxidation of Alkenes by Palladium(II)- and Rhodium(III)-Nitro Complexes.

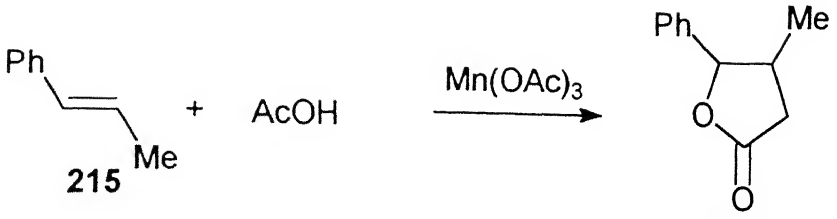
Andrews and coworkers have recently shown that bis(acetonitrile)(chloro)(nitro) palladium(II) stoichiometrically reacts with terminal alkenes to give the corresponding methylketone in almost quantitative yield and a reduced $[PdCl(NO)]_n$ complex. When the same reaction is carried out in the presence of dioxygen, a slightly catalytic production of 2-alkanone occurs(2-7 turnovers) [84]. The ketonic oxygen comes from the coordinated nitro group.

The cationic rhodium(II)-nitro complex $[(MeCN)_4RhNO_2]^{2+}(BF_4)_2$ also oxidizes ethylene and 1-octene to acetaldehyde and 2-octanone, respectively. However, no catalytic oxidation takes place in the presence of dioxygen[85].

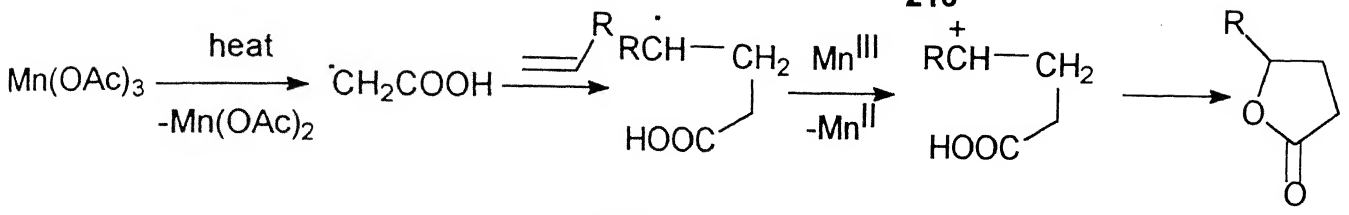
6.1.3 Manganese

The stoichiometric oxidation of alkenes by $Mn(OAc)_3$ in acetic acid at 120° C affords γ-lactones in good yields, via the homolytic addition of carboxymethyl radical to the

double bond (Eq. 36 and Scheme 44)[86-88].

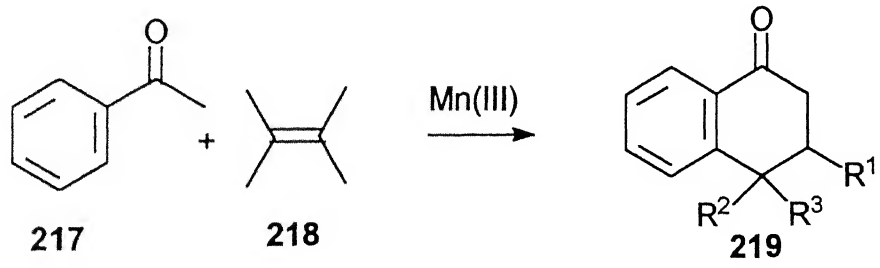


Eq. 36



Scheme 44

In a similar manner, ketones, esters and aldehydes are also oxidized by Mn(III) acetate to give β-oxoalkyl radicals that can add to alkenes to form a variety of interesting products. Substituted α-tetralones **219** have been synthesized by Mn(III) promoted addition of aromatic methyl ketone **217** to various alkenes (Scheme 45).



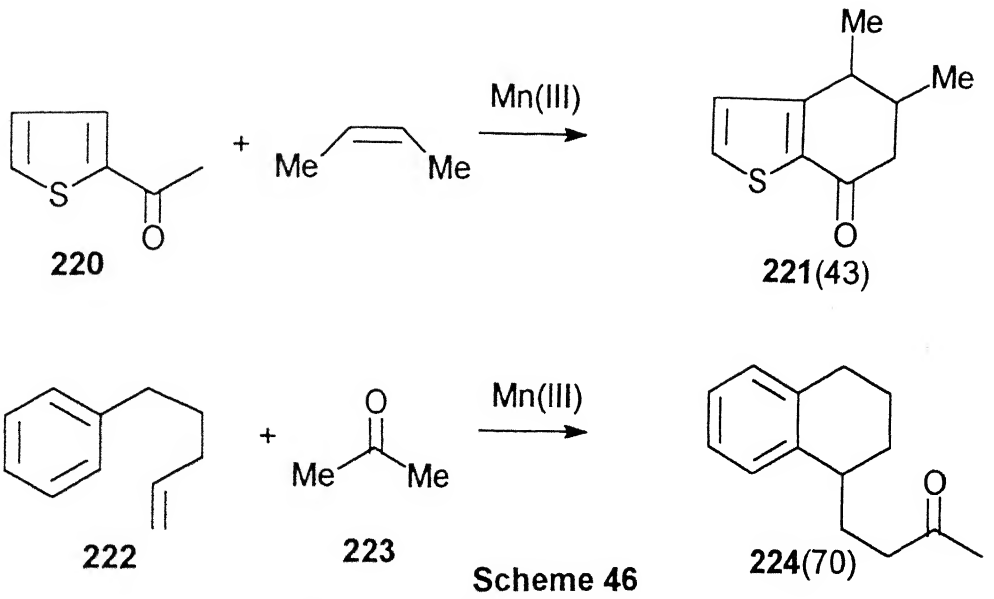
a) $R^1=R^2=H$, $R^3=Et$ — a) 49%

b) $R^1=H$, $R^2=R^3=Me$ — b) 43%

c) $R^1=R^3=Me$, $R^2=H$ — c) 40%

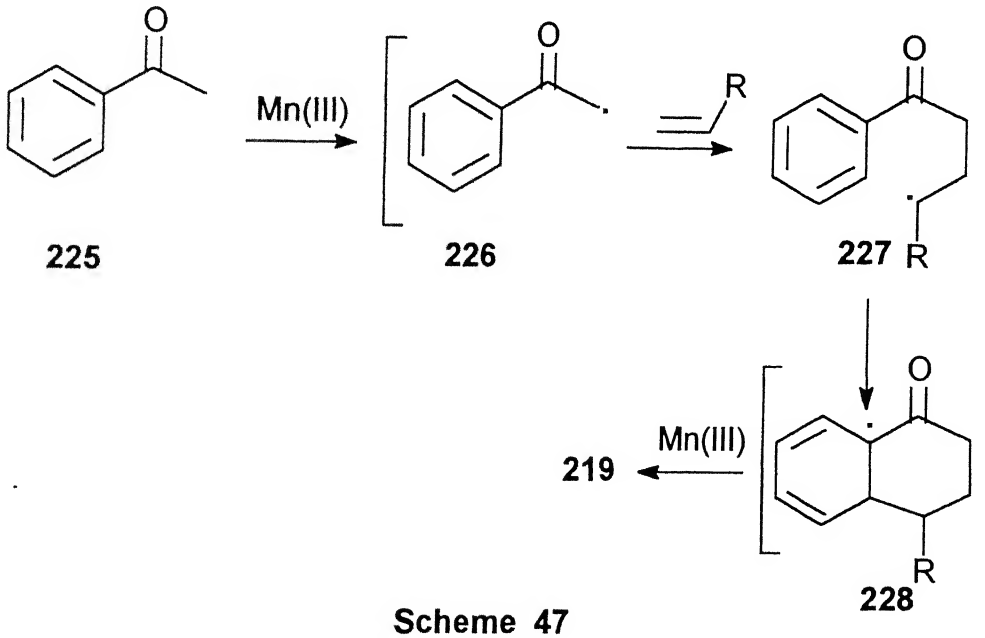
Scheme 45

Similarly, the synthesis of **221** and **224** can be achieved using methyl ketone **220** derived from thiophene or by addition of acetone **223** to aromatic alkenes **222** (Scheme 46).



Scheme 46

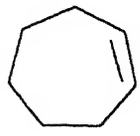
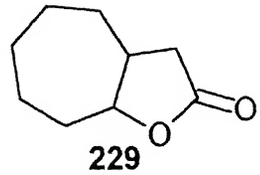
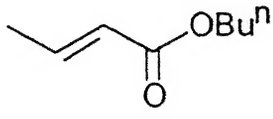
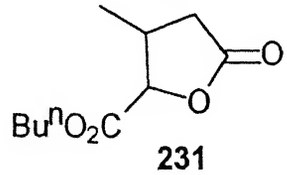
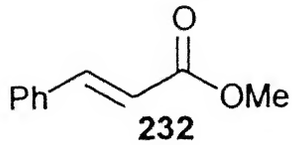
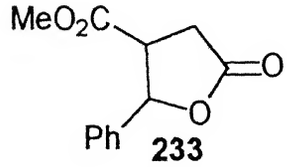
These reactions are considered to proceed via a radical process where Mn(III) initiates the oxidation of methyl ketone to give **226** which undergoes intermolecular addition to the alkenes to produce a new radical **227**. Intramolecular addition of radical **227** to aromatic ring gives rise to a stabilized radical **228** which is oxidized with Mn(III) to restore the aromaticity and yield the tetralone or tetralin **219, 221** and **224** respectively (Scheme 47).



Scheme 47

The pioneering work of Fristad and coworkers[89-95] have highlighted the synthesis of variety of γ-lactones from carboxylic acids and alkenes (Table 24)[89]. These workers have also

Table 24. Mn(III) Promoted Synthesis of γ-Lactones from Acetic acid and Alkenes

Entry	Alkene	Product(s) Yield(%)	cis:trans
1		 **229**	1:24
2	 **230**	 **231**	1:38
3	 **232**	 **233**	1:26

a) Only major products are mentioned here

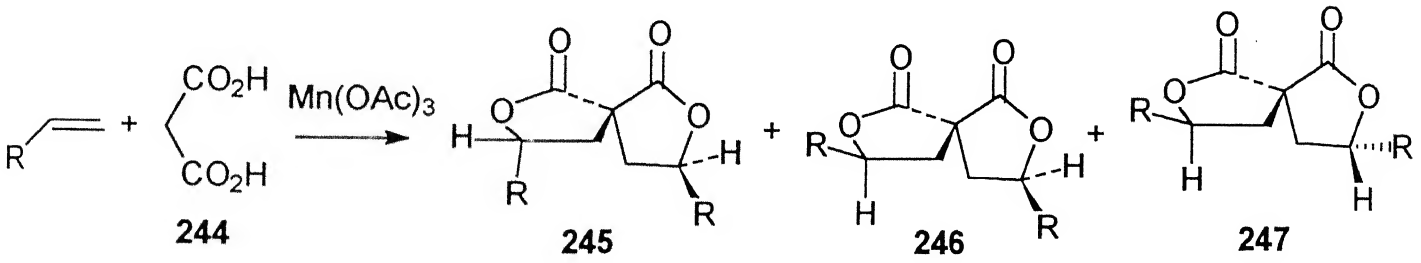
shown that chloroacetic acid, 3-chloropropionic acid and cyanoacetic acid can be converted into the corresponding lactones in high yields (Table 25)[91]. Mn(III) acetate promoted oxidation of malonic acid in the presence of alkenes results in the formation of spiro-fused lactones, 2,7-dioxaspiro[4,4]nonane-1,6-diones **245-247** (Scheme 48).

Under appropriate conditions, manganese(III) acetate can be used as a free-radical initiator for the homolytic addition of acetic anhydride to terminal alkenes. Linear or α-branched carboxylic acids can be produced in good yields based on α-alkenes[96].

In the presence of bromide, the oxidation of alkenes by $Mn(OAc)_3$ in acetic acid readily occurs at 70-80°C and produces allylic acetates in good yields. Thus, cyclohexene is oxidized to

Table 25. Mn(III) Promoted Lactonisation using Chloroacetic, 3-Chloropropanoic and Cyanoaceatic acids and Alkenes

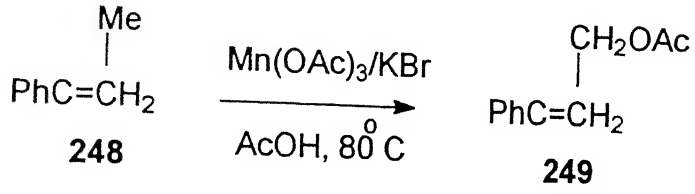
Entry	Acid	Alkene	Lactone(yield %)[a] α,β-Unsaturated, γ-lactones	
1	$ClCH_2CO_2H$ **234**	$H_{17}C_8$ **237**	Cl, $H_{17}C_8$ **238**	$H_{17}C_8$ **241**
2	$ClCH_2CH_2CO_2H$ **235**		Cl, $H_{17}C_8$ **239**	$H_{17}C_8$ **242**
3	$NCCH_2CO_2H$ **236**		CN, $H_{17}C_8$ **240**	$H_{17}C_8$ **243**



R	Yield(%)	Ratio(**245:246:247**)
$C^n{}_4H_9$	100	9:47:44
$C^n{}_6H_{13}$	100	11:59:30
Bu^t	42	2:48:50
CH_2Cl	30	9:60:31

Scheme 48

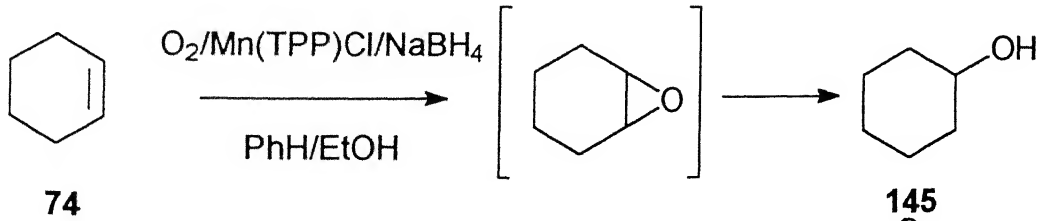
cyclohexenyl acetate[97] and α-methylstyrene **248** to β-phenylallyl acetate[98] , **249** with a mechanism involving allylic hydrogen abstraction by bromide atoms coming from the oxidation of bromide by Mn(III) (Eq. 37).



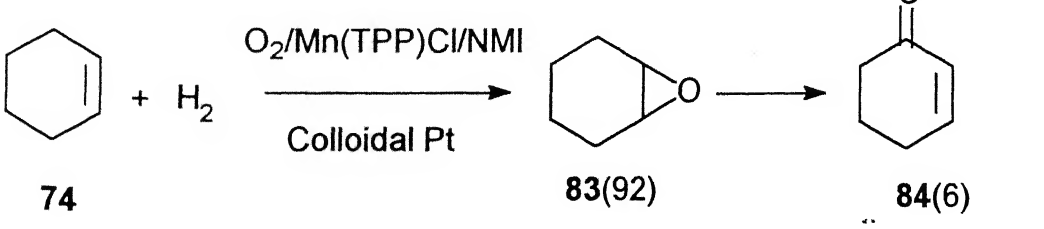
Eq. 37

Manganese Porphyrins

Tabushi and coworkers reported that oxygenation of cyclohexene **74** in the presence of Mn(TPP)Cl and sodium borohydride unusually produced cyclohexanol **145** as the major product, while the same reaction was carried out in the absence of sodium borohydride afforded the conventional radical autoxidation products. Since cyclohexene oxide was readily transformed into cyclohexanol under the reaction conditions, it was reasonably suggested that the epoxide is the primary product of the reaction (Eq. 38)[99]. Later, the same authors were able to stop the reaction at the epoxide stage by using Mn(TPP)Cl, 1-methylimidazole (NMI), O_2 and (H_2+Colloidal platinum) as the coreducing agent (Eq. 39)[100]. Although a substantial amount of water was directly produced from the reaction of O_2+H_2, epoxide was catalytically formed



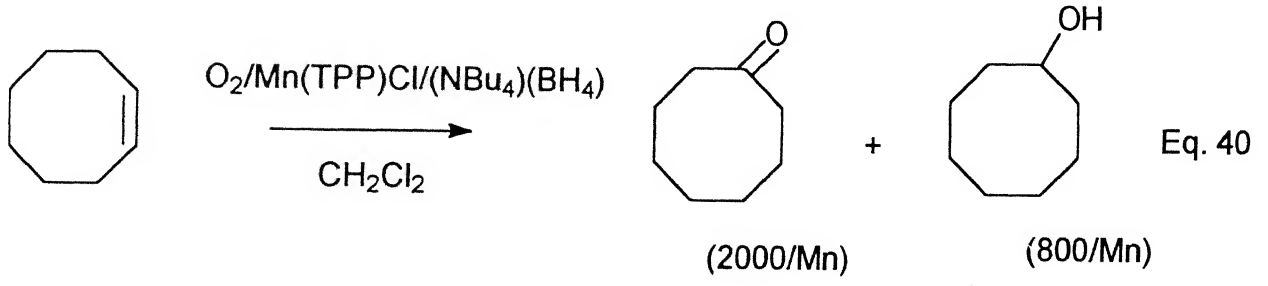
Eq. 38



Eq. 39

with respect to manganese (65 turnovers) and platinum (300 turnovers). The reactivity order of alkenes i.e., increasing with their nucleophilic nature, was found to be similar to that observed with a related Mn(TPP)Cl/PhIO catalytic epoxidation system. In contrast to this PhIO system, the epoxidation of alkenes with O_2+H_2 proceeds with retention of configuration (eg. cis-alkenes gave cis-epoxides only).

Surprisingly, different oxidation of alkenes was found to occur in the presence of Mn(TPP)Cl catalyst and $[NBu_4][BH_4]$ coreducing agent[101]. Except for cyclohexene (transformed into cyclohexen-3-ol and cyclohexanol), the other alkenes, viz. cyclooctene, styrene and 1-octene, were transformed into the corresponding ketone and the ensuing alcohol hydrogenation product (Eq. 40).



Eq. 40

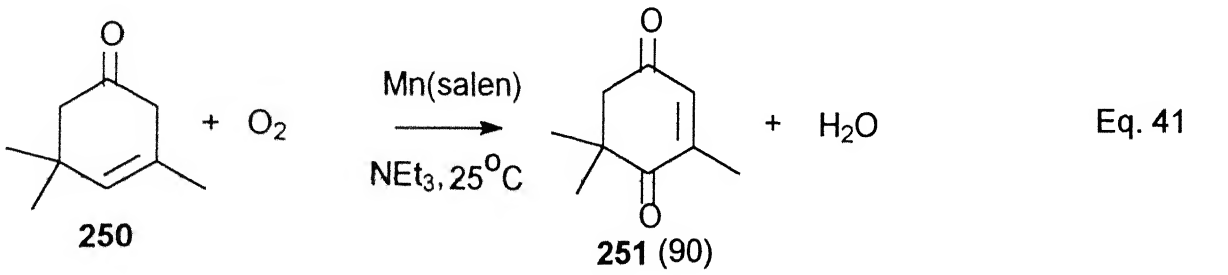
In the presence of ascorbate coreducing agent and under phase-transfer conditions, manganese porphyrins have recently been shown to activate oxygen by catalyzing epoxidation of alkenes and hydroxylation of alkanes to the corresponding alcohol and ketones mixtures.[102]

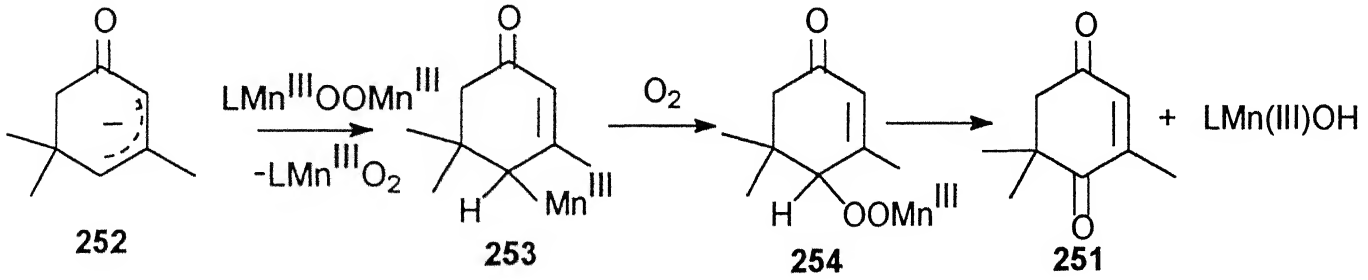
Miscellaneous Manganese Catalyzed Oxidations

Catalytic oxidations using manganese complexes and dioxygen. Although reversible dioxygen adducts of the superoxo or peroxo type have been detected by the interaction of manganese(II) porphyrin or Schiff base complexes with dioxygen at low temperature[10] or from the reaction of $MnX_2(PR_3)$ (X=Cl, Br, I) with oxygen[103] no reactivity towards hydrocarbons has

been reported.

β-Isophorone can be oxidized by air to 1,5,5-trimethylcyclohexene-3,6-dione in the presence of Mn(salen) and triethylamine (Eq. 41 and Scheme 49)[104]. The mechanism suggested involves carbanion **252** formation from the reaction of triethylamine with β-isophorone, followed by the formation of an alkyl peroxide-manganese(III) complex **253** which decomposes to the dienone **254**.[104,105]





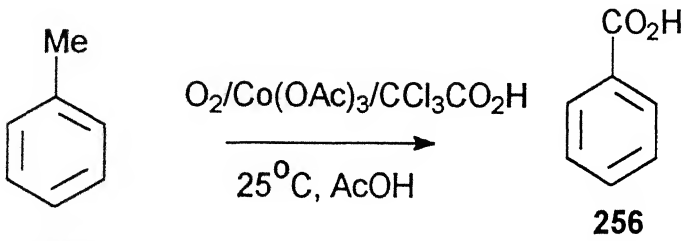
Scheme 49

6.1.4 Cobalt Catalysts

6.1.4.1 Oxidation by cobalt(III) salts

The oxidation of hydrocarbons by cobalt(III) acetate has been thoroughly investigated, due to its relevance to industrial homolytic oxidation processes[105-107]. These oxidations are dramatically accelerated by the presence of strong acids or halide salts.

Oxidation of alkenes by $Co(OAc)_3$ preferentially occurs at the allylic positions, yielding 2-alkenyl acetate. Oxidation of cyclohexene by cobalt(III) acetate and trifluoroacetic acid in acetic acid results in the formations of cyclohexenyl acetate along with minor amounts of the corresponding allyl alcohol[108]. The oxidation of ethylene by cobalt(III) trifluoroacetate in trifluoroacetic acid affords glycol bis(trifluoroacetate)[109]. Oxidation of alkylbenzene by cobalt(III) acetate mainly occurs at the side chain benzylic positions, without formation of nuclear adducts. In nitrogen, benzylic acetate predominate, whereas aromatic acids are favored when oxygen is present[110]. Thus, toluene is transformed into benzyl acetate and benzaldehyde by cobalt(III) acetate in acetic acid under anaerobic conditions.[111] When this reaction is carried out in the presence of dioxygen and trichloroacetic acid, benzoic acid is almost exclusively formed with relatively high turnover numbers (Eq. 42).[110]

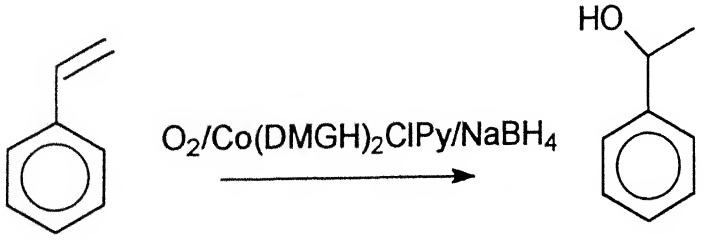


255 **256** Eq. 42

6.1.4.2 Catalysis by Cobalt Porphyrins and Schiff Base Complexes

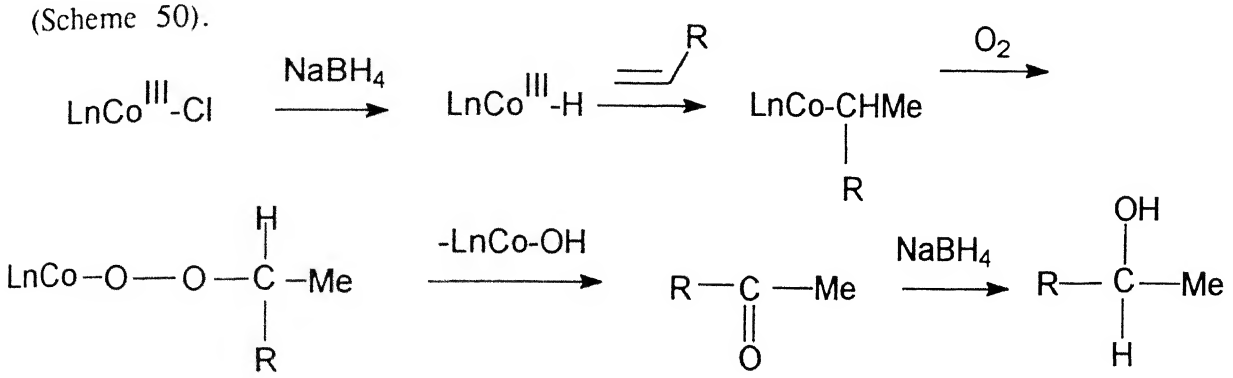
Oxidation of terminal alkenes by dioxygen and a coreducing agent

Styrene derivatives can be selectively converted to the corresponding benzyl alcohol by dioxygen in the presence of bis(dimethylglyoximato)chloro(pyridine)cobalt(III) and sodium tetrahydroborate (Eq. 43)[111].



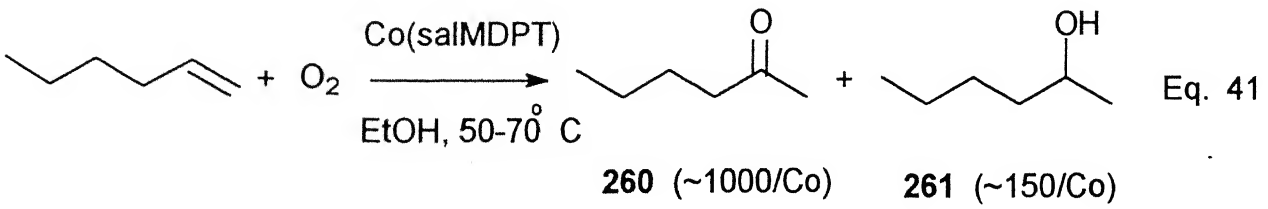
257 **258** Eq. 43

A likely mechanism for this reaction involves insertion of the alkene into the cobalt-hydride bond, followed by dioxygen insertion into the cobalt-carbon bond, and decomposition of the peroxide adduct to the ketone, which is reduced to alcohol by sodium borohydride (Scheme 50).



Scheme 50

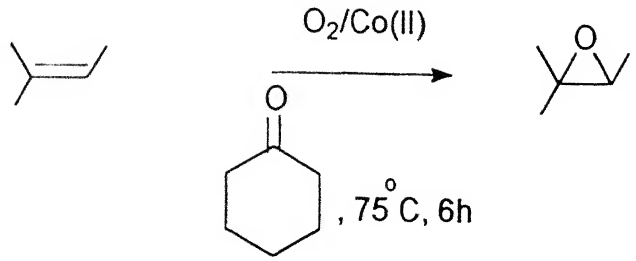
A somewhat similar oxidation of terminal alkenes to methyl ketone and alcohol by dioxygen in the presence of Co(SalMDPT)[SalMDPT=bis(salicylideneiminopropyl)methyl-amine] and in ethanol solvent has recently been reported by Drago and coworkers (Eq. 44).[112] Only terminal alkenes were found to be reactive with this catalytic system. The reaction occurs ethanol or methanol but not in t-butyl or isopropyl alcohols. The alcohol is concomitantly oxidized during the reaction, and may act as a coreducing agent and / or favor the formation of cobalt hydride. This oxidation might occur according to the mechanism presented in scheme 50.



260 (~1000/Co) **261** (~150/Co)

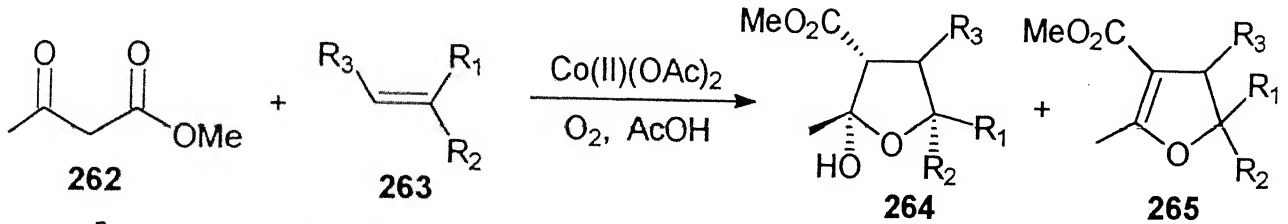
Eq. 41

Very recently Mukaiyama and coworkers have shown that cobalt(II) Schiff base complexs Co(4-Meo-Saloph), Co(acac) and Co(AMeDPT) were found to be catalysts in epoxidizing trisubstituted alkenes in the presence of carbonyl compounds and dioxygen at 100°C (Eq. 45).[113]



Eq. 45

Recently, in our laboratory, it has been observed that cobalt(II) acetate mediate the reaction of 1,3-dicarbonyl compounds with unactivated alkenes only in the presence of dioxygen to give the corresponding tetrahydrofuran or dihydrofuran derivatives in good yields (Scheme 51)[114].

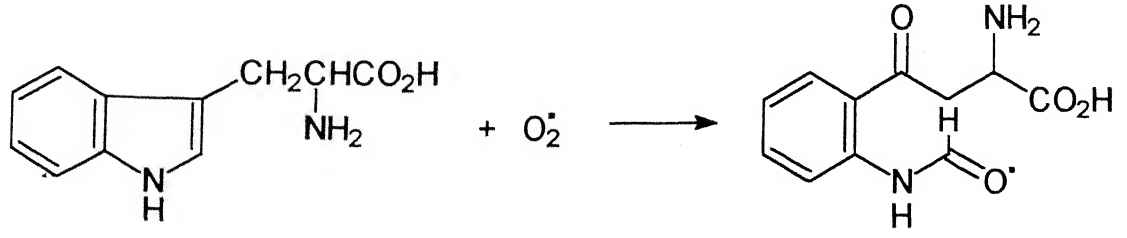


a) $R_1 = {}^nC_6H_{13}$, $R_2 = R_3 = H$ — 60% — -
b) $R_1 = {}^nC_{10}H_{21}$, $R_2 = R_3 = H$ — 70% — -
c) $R_1 = {}^nC_5H_{11}$, $R_2 = H$, $R_3 = CH_3$ — - — 58%

Scheme 51

6.1.4.3 Oxidative Cleavage Reactions

Cobalt(II) Schiff base complexes eg. Co(salen)[115], Co(acacen)[116] and cobalt(II) porphyrins[117] eg. Co(TPP), are effective catalysts for the selective oxygenation of 3-substituted indoles to ketoamides (Eq. 46), a reaction which can be considered as a model for the heme-containing enzyme tryptophan-2,3-dioxygenase (Eq. 18)[119].



(Eq. 18)

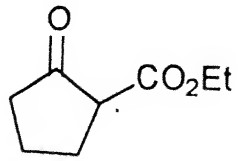
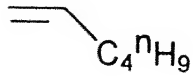
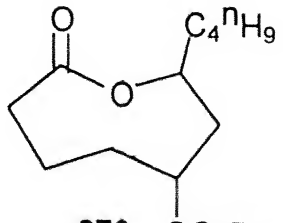
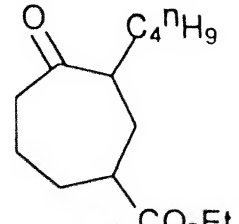
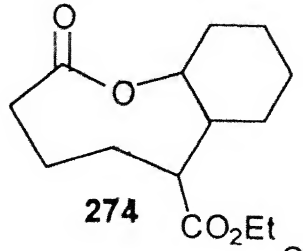
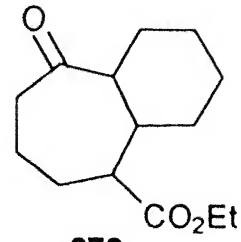
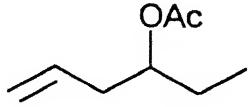
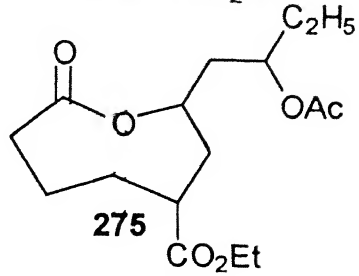
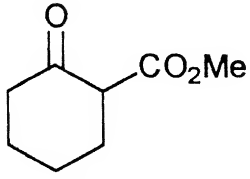
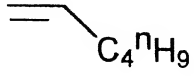
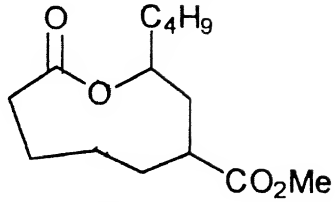
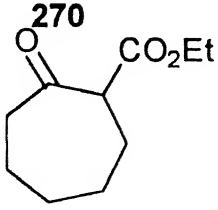
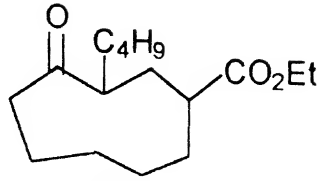
6.2 Present Study

In view of the importance of metal catalyzed oxidation of organic compounds with dioxygen, we have carried out a detailed investigation on cobalt(II) Schiff base complexes catalyzed oxidation of organic compounds with dioxygen in the presence of 1,3-dicarbonyl compounds which act as reducing agents. The following sections deal with the generation of 1,3-dicarbonyl radical and subsequent reactions with different organic substrates, such as addition with alkenes, epoxidation, allylic oxidation, benzylic oxidation and alcohol oxidation in the presence of dioxygen and cobalt(II) Schiff base complexes.

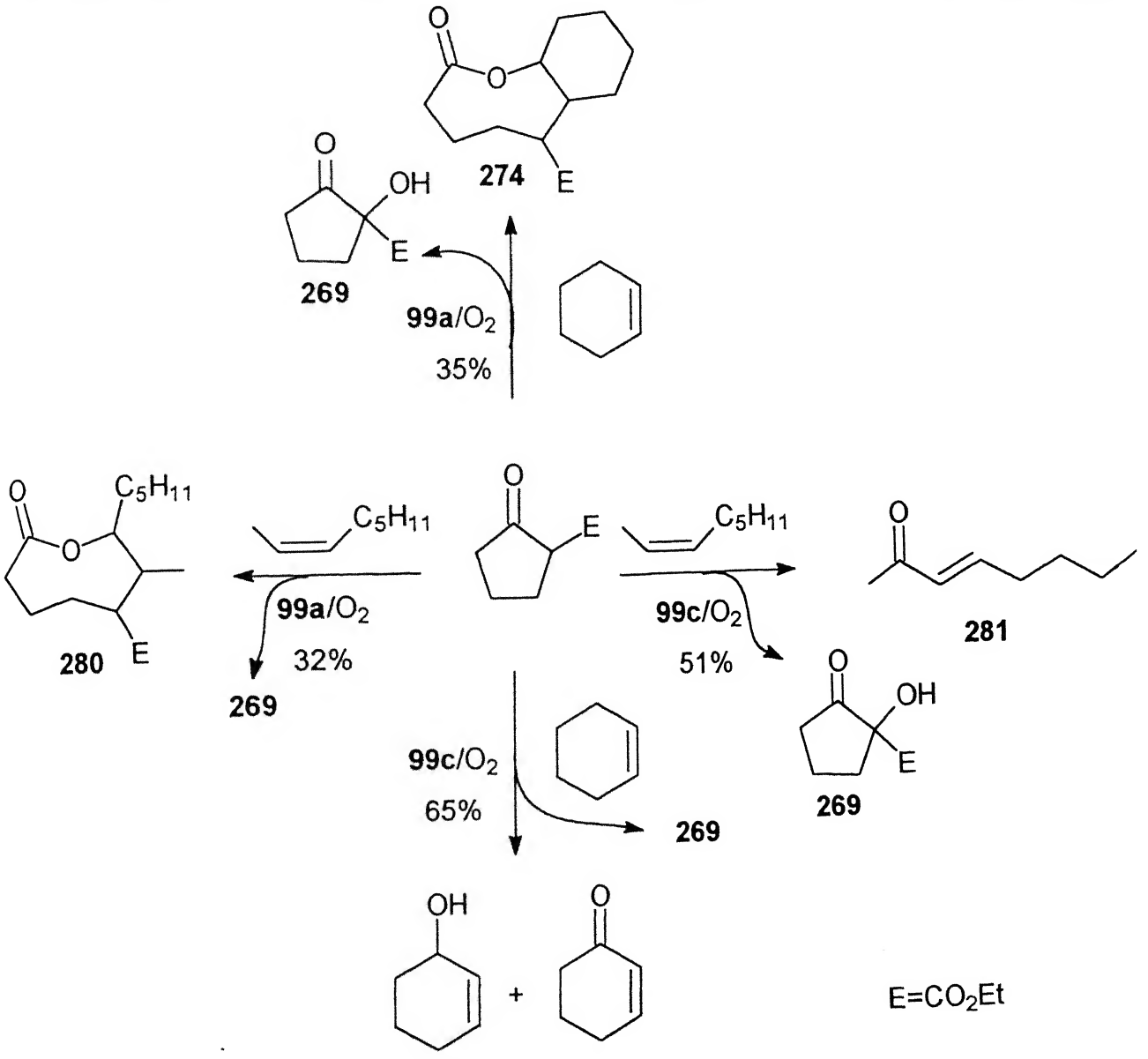
6.2.1 Cobalt(II) Catalysed Oxidative Addition Reaction of β-Ketoesters with Alkenes in the Presence of Dioxygen

The reaction of β-ketoester with various alkenes in the presence of cobalt catalysts **99a-99c** showed very interesting reactivity profile. Thus, the reaction of β-ketoester **268** with 1-hexene in the presence of dioxygen is catalyzed by cobalt complex **99a** to give a mixture of eight membered lactone **273** and substituted cycloheptanone **277** derivative (Table 26, Entry 1). A similar treatment of β-ketoester **268** with cyclohexene **74** afforded a mixture of lactone **274** and macrocyclic ketone **278** in moderate yields (Table 26, Entry 2). The homoallylic acetate **272** reacted under similar reaction conditions to give the corresponding eight membered lactone **275** as major product (Table 26, Entry 3). In this case no substituted cycloheptanone derivative was observed. The reaction with six membered β-ketoester **270** and n-hexene provided the corresponding nine membered lactone **276** as the sole product in moderate yield. Similarly, seven membered β-ketoester **271** afforded the nine membered cyclic ketone **279** as the exclusive product in low yield. These reactions are not accompanied by any corresponding epoxide as the by product. In these reactions, the corresponding tertiary alcohol **269** was obtained as by-product.

Table 26. Cobalt (II) Catalysed Reaction of β-Ketoesters with Various Alkenes in the Presence of Dioxygen

Entry	1,3-Dicarbonylcompound	Alkene	Catalyst	Product	(% yield)[b]
1	 **268**		**99a**	 **273**  **277**	49(4:1)
2	 **74**			 **274**  **278**	40(4 :0.5)
3	 **272**			 **275**	40(1:0)
4	 **270**			 **276**	44(1:0)
5	 **271**		-	 **279**	29(0:1)

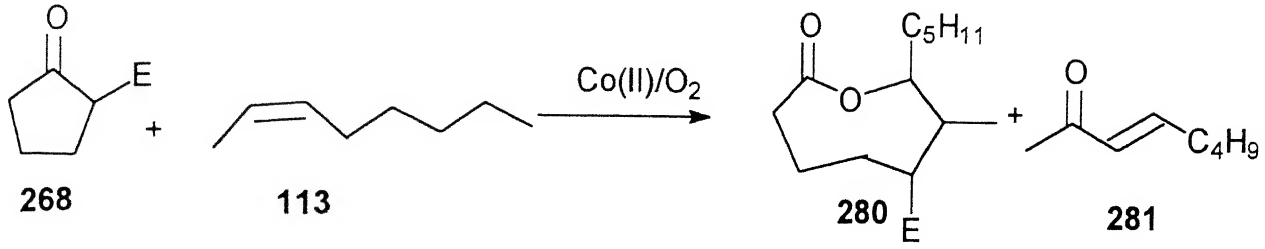
On the other hand, the reaction of cis-2 octene and methyl 2-oxocyclopentanecarboxylate **268** in the presence of catalyst **99c** affords **281** as the major product, however, when the reaction was carried out with catalyst **99a** a mixture of products were obtained, out of which, the eight membered lactone **280** was obtained in moderate yield (Scheme 52). Interestingly,



Scheme 52

when the catalyst **99b** was used, a mixture of enone **281** and corresponding lactone **280** was observed in moderate yield. This diverse pattern of reactivity may be arising due to the difference in the ligands **98a-c** present in these catalysts **99a-c** (Table 27, Entry 1-3).

Table 27. Cobalt(II) Catalysed Reaction of cis-2-Octene in the Presence of Dioxygen

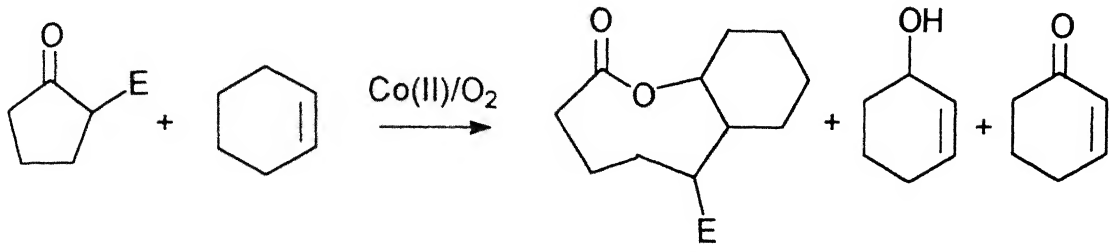


268 113 280 281

Entry	Catalyst	Product(%yield)	
		280	281
1	**99a**	32	-
2	**99b**	11	42
3	**99c**	-	51

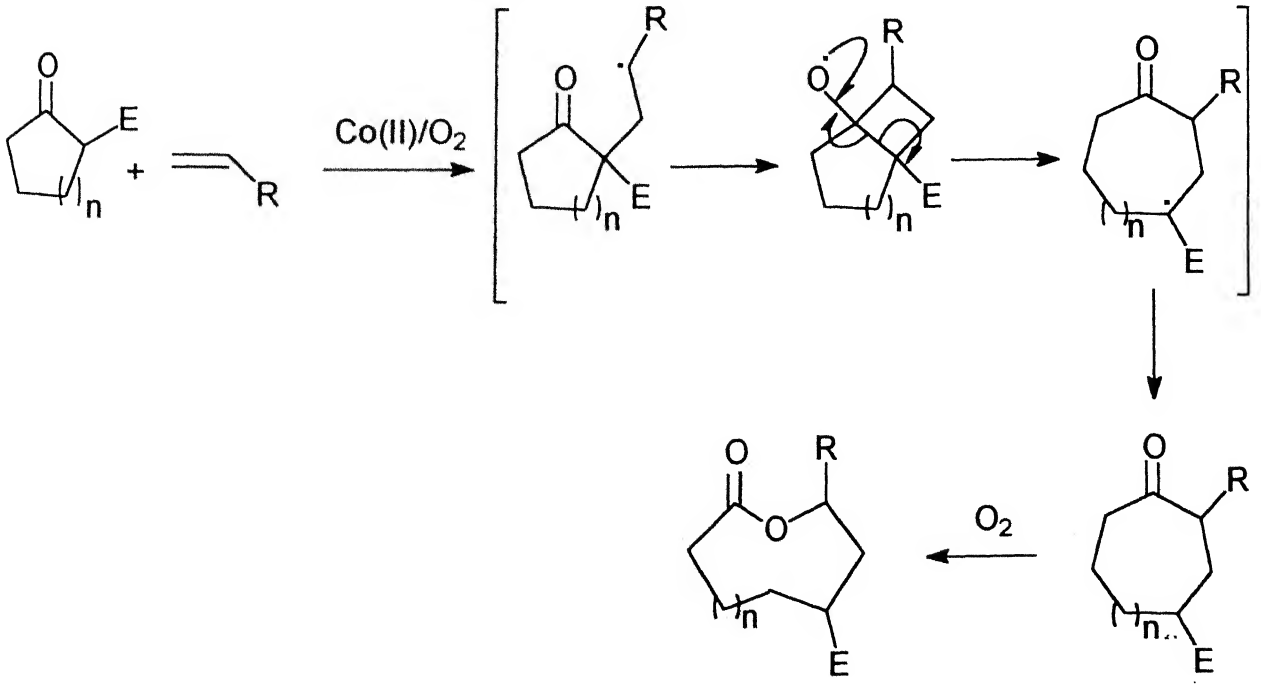
Interestingly, cyclohexene is also exhibited a similar kind of reactivity profile as cobalt(II) complex **99c** converts it into the corresponding cyclohexenol in good yield whereas catalyst **99a** catalyses the oxidative addition of ketoester to provide the eight membered lactone **274** as the major product (Table 28, Entries 1-3, Scheme 52). The formation of lactone may be proceeding by Baeyer Villiger oxidation of the corresponding ketone. Ketone may be formed by a sequence of intermolecular addition of ketoester to alkene followed by intramolecular cyclization and rearrangement as shown in the Scheme 53. Intramolecular cyclization to give a 4-membered ring (4-exo-trig) is not precedented, however, the presence of cobalt may direct this unfavorable cyclization.

Table 28. Cobalt(II) Catalysed Reaction of Cyclohexene in the Presence of Dioxygen



268 **74** **274** **116** **84**

Entry	Catalyst	Product(% Yield)	
		274	**116 & 84**
1	**99a**	35	11
2	**99b**	-	62
3	**99c**	-	65



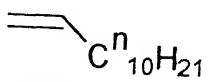
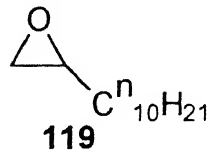
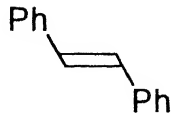
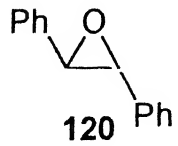
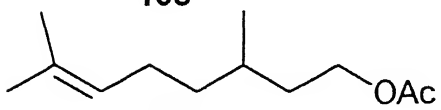
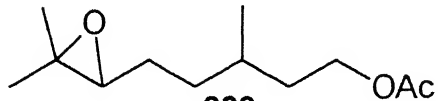
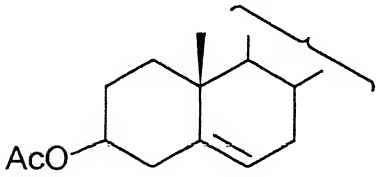
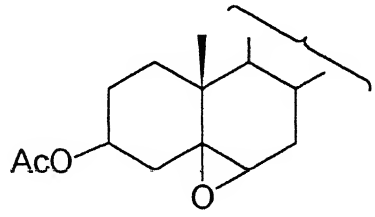
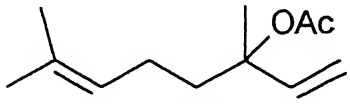
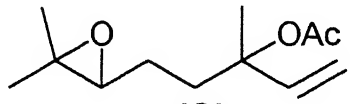
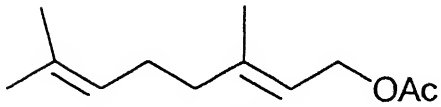
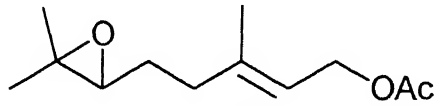
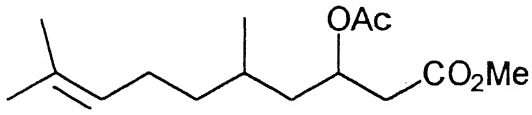
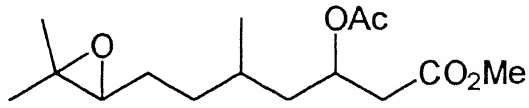
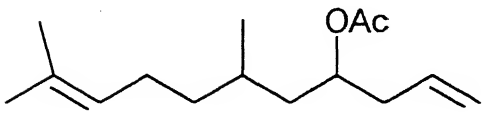
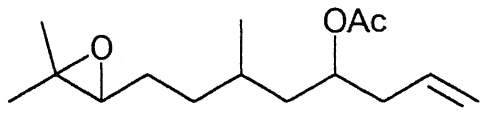
Scheme 53

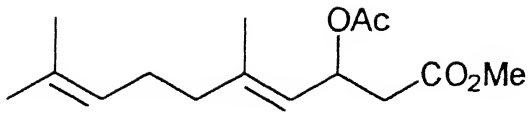
6.2.2 Epoxidation of Unactivated Alkenes in the Presence of Dioxygen

The cobalt(II) complex **99c** catalyses the reaction of unactivated alkenes in the presence of methyl 2-oxocyclopentanecarboxylate and dioxygen to afford the corresponding stereo- and regioselective expoxides in good yields. In this reaction, β-ketoester was transformed to the corresponding tertiary alcohol in quantitative yield. This process was facilitated by various Schiff base catalysts **99b-99d, 298** and **299** (Table 31).

A wide range of alkenes are prone to epoxidation under these conditions with high stereo- and regioselectivity. Regioselective epoxidation of monoenes and dienes can be achieved as indicated by the selective conversion of these to the corresponding mono epoxides (Table 29, Entries 1-9). Interestingly, the regioisomeric epoxide and diepoxide were not observed under these conditions and in case where the chemical yields are not high, the unchanged starting alkenes were recovered (Table 29, Entries 7-9). It is noteworthy that the more substituted double bond is epoxidised whereas terminal and allylic double bonds are not affected during this transformation. Similarly, selective mono epoxidation of a triene can also be achieved in moderate yield and again no regioisomeric epoxide was observed in this case (Table 29, Entry 10). These epoxides were obtained as a mixture of diastereomers, however, no attempt was made to separate them or ascertain their relative ratios. The α-isomer of cholesteryl acetate epoxide was obtained as major product in the presence of catalyst **99c** (Table 29, Entry 4). The epoxidation of cholesteryl acetate can also be performed by methyl 2-methylacetoacetate and methyl 2-oxocyclohexanecarboxylate and the results from these epoxidations were quite comparable. Interestingly, α-pinene underwent smooth epoxidation to give **294** as the major product (Table 29, Entry 11) whereas, enolsilane of cyclohexanone **288** underwent oxidation to the corresponding 2-hydroxycyclohexanone **295** in good yield (Table 29, Entry 12).

Table 29. Cobalt(II) Catalysed Epoxidation of Unactivated Alkenes with Dioxygen

Entry	Alkene	Product	% Yield
1	 **112**	 **119**	62
2	 **108**	 **120**	64
3	 **282**	 **289**	69
4	 **127**	 **129**	77
5	 **115**	 **123**	71
6	 **87**	 **88**	49
7	 **283**	 **290**	32
8	 **284**	 **291**	29

9 

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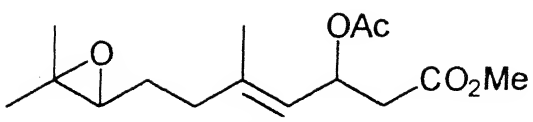
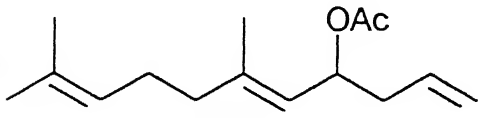


292

10 

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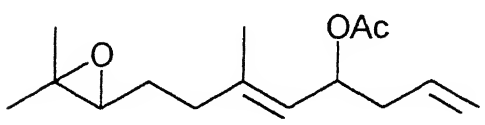
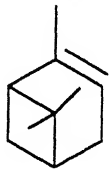


293

11 

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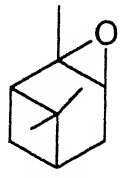

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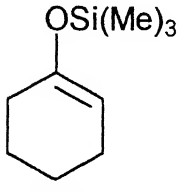
12 

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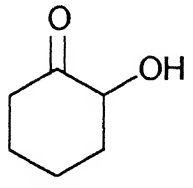
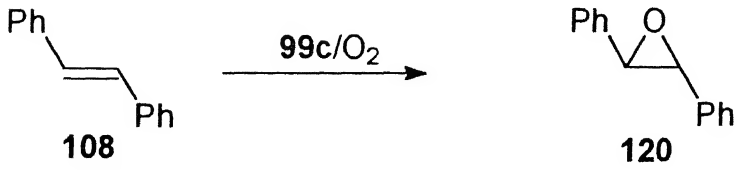


295

Epoxidation of trans-stilbene **108** was carried out by different carbonyl compounds in the presence of molecular oxygen and catalyst **99c**, ethyl 2-oxocyclopentanecarboxylate **268**, methyl 2-oxocyclohexanecarboxylate **270** and methyl 2-methylacetoacetate **296** were found to be better coreducing agents whereas cyclohexanone gave less yield. Methyl ethyl ketone and methyl 2-allyl acetoacetate **297** did not react under these reaction conditions (Table 30, Entries 1-6).

Epoxidation of trans-stilbene was also carried out in the presence of ethyl 2-oxocyclopentanecarboxylate **268** and dioxygen using different catalysts **99b-c, 298** and **299**. All the catalysts gave the corresponding trans epoxide with comparable yields, however, the catalysts **99b-c** and **299** derived from α-amino acid ester and aromatic aldehydes gave better results whereas cobalt salophen **298** afforded **120** in moderate yield (Table 31, entries 1-5)

Table 30. Cobalt(II) Catalysed Epoxidation of (E)-Stilbene in the Presence of Dioxygen



108 **120**

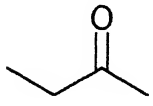
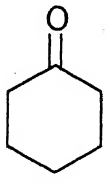
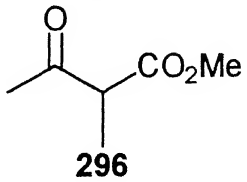
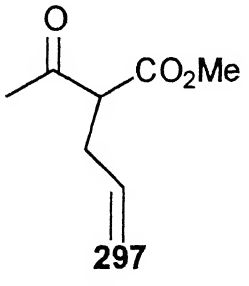
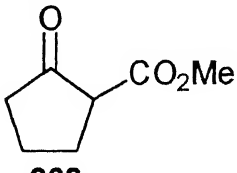
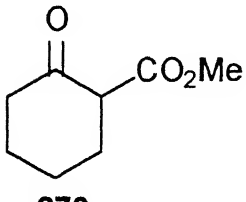
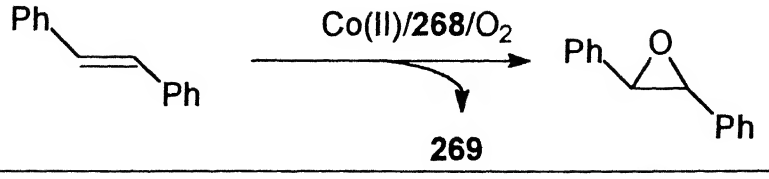
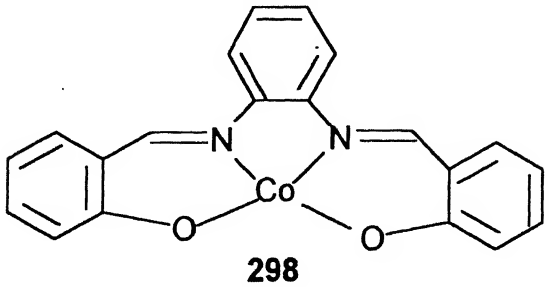
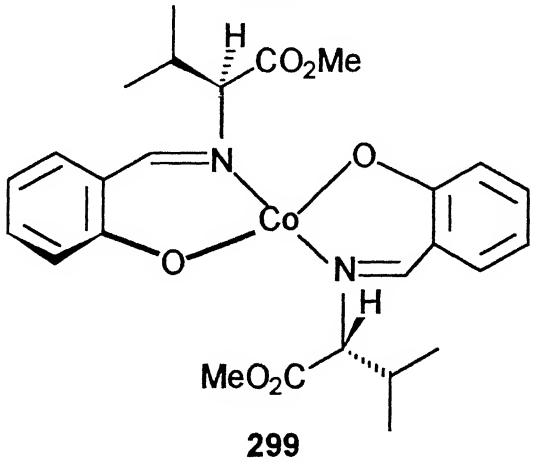
Entry	Ketone/Ketoester	Product (% yield)
1		no reaction
2		<10
3	 **296**	65
4	 **297**	no reaction
5	 **268**	61
6	 **270**	70

Table 31 Effect of Catalysts on the Epoxidation of (E)Stilbene



269

Entry	Catalyst	Product(% yield)
1	 **298**	42
2	 **299**	59
3	**99b**	55
4	**99c**	64
5	**99d**	57

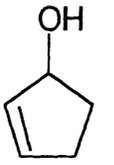
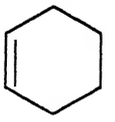
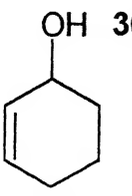
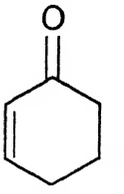
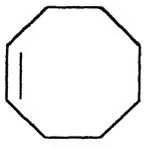
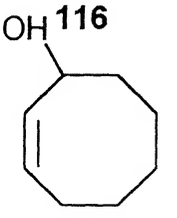
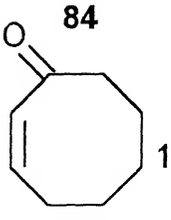
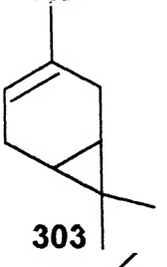
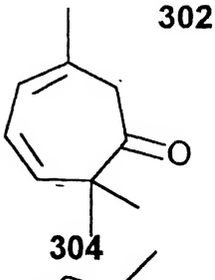
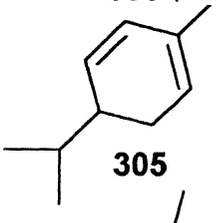
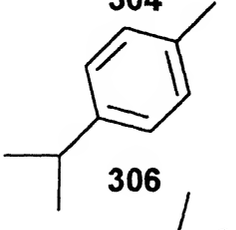
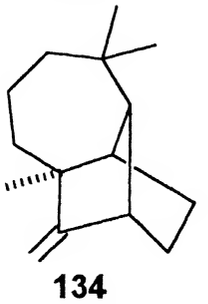
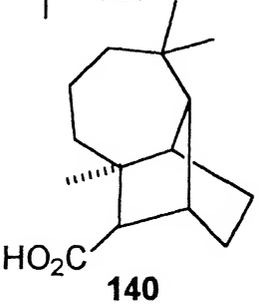
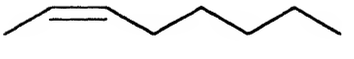
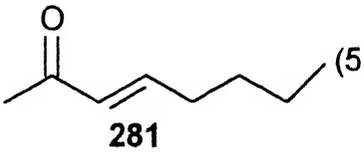
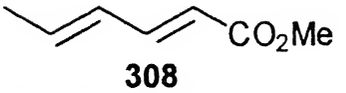
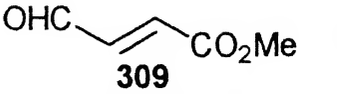
6.2.3 Allylic Oxidation of Alkenes in the Presence of Dioxygen

Surprisingly, the reaction with cyclic alkenes in the presence of **99c** did not afford any epoxides, however, the corresponding allyl alcohol or enones are obtained as the major products (Table 32, entries 1-8). Thus, cyclopentene was mainly converted to the corresponding alcohol whereas cyclohexene and cyclooctene were oxidized to a mixture of corresponding alcohols and ketones respectively (Table 32, Entries 1-3). Interestingly, Δ^3-carene underwent a radical induced rearrangement to afford a cycloheptadienone in quantitative yield (Table 32, Entry 4, Scheme 54). Similarly, R(-)-α-Phellandrene underwent aromatization to afford p-cymene in very high yield. Interestingly, (+)-longifolene underwent oxidation to the corresponding carboxylic acid, this may be formed by the isomerization of the epoxide to aldehyde which may further be oxidized to the corresponding carboxylic acid in the reaction medium (Scheme 55). (Z)-2-Octene also exhibited allylic oxidation rearrangement followed by oxidation to give enone with exclusive (E)-geometry (Scheme 56). A careful study of the reaction mixture revealed the absence of the corresponding (Z)-isomer, however, apart from the enone an unidentified product ($\sim$30 %) was also obtained after column chromatography. Methylsorbate underwent cleavage of the double bond under this reaction conditions to give the functionalized aldehyde as the major product.

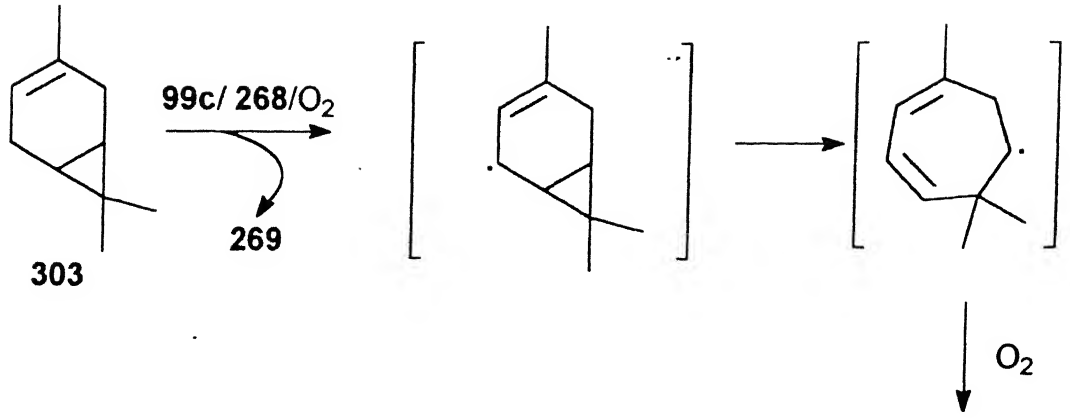
6.2.4 Benzylic Oxidations in the Presence of Dioxygen

Benzylic substrates also underwent oxidation to the corresponding ketones under the above mentioned experimental conditions. Thus, diphenyl methane, ethyl benzene, tetralin and fluorene were oxidized by the following protocol to afford the corresponding ketones in good

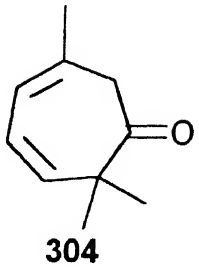
Table 32. Cobalt(II) Catalysed Allylic Oxidations with Molecular Oxygen

Entry	Alkene	Product	(% yield)[a]
1		 **300**	(71)
2	 **74**	 **116**  **84**	2:1 (65)[b]
3	 **132**	 **301**  **302**	1:1 (56)[b]
4	 **303**	 **304**	(67)
5	 **305**	 **306**	(69)
6	 **134**	 **140**	(53)
7	 **113**	 **281**	(51)
8	 **308**	 **309**	(67)

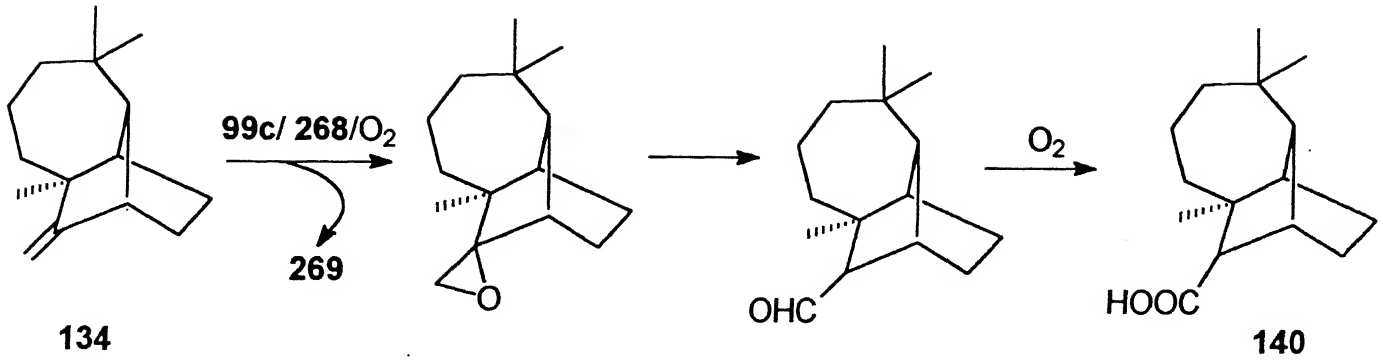
[a]Isolated yield. [b] *Ratio determined from the ^1H NMR of the crude reaction mixture.*



Scheme 54

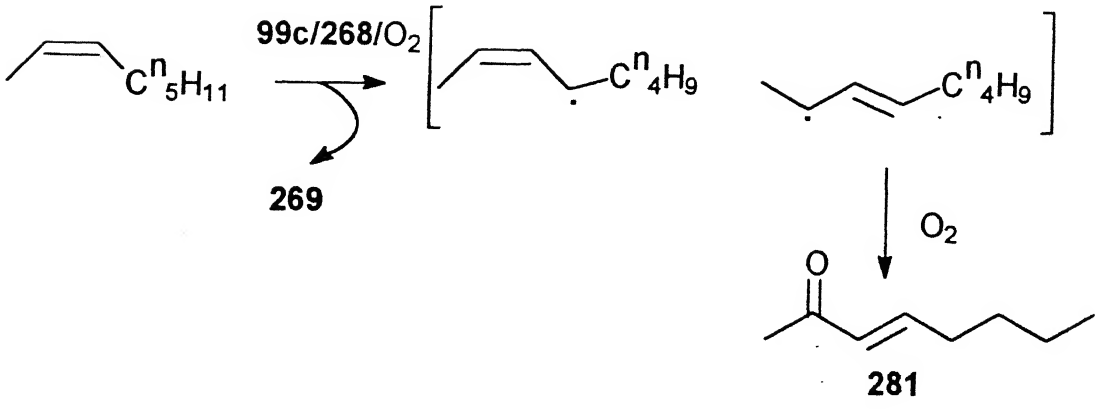


304



134 140

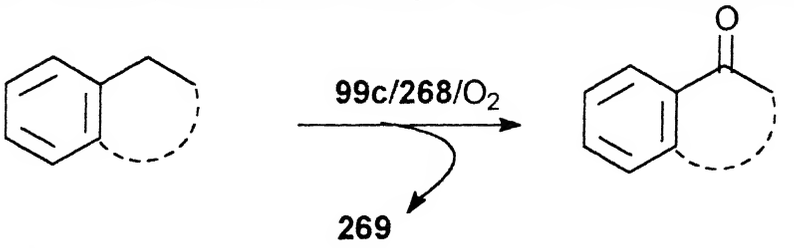
Scheme 55

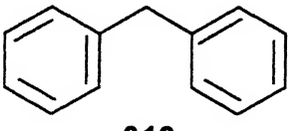
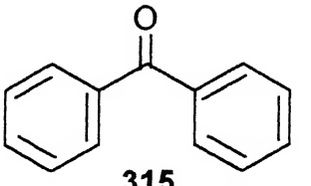
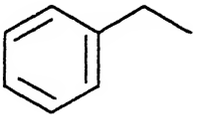
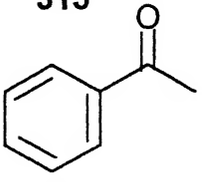
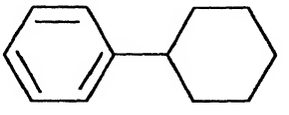
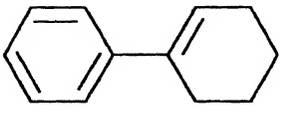
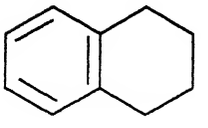
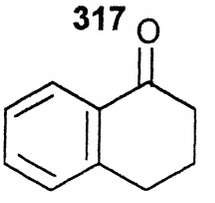
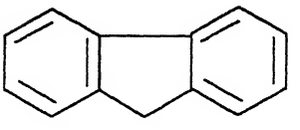
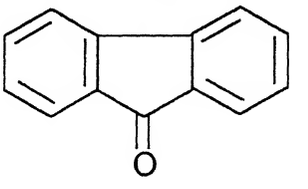


281

Scheme 56

Table 33 . Cobalt(II) Catalysed Benzylic Oxidations with Dioxygen



Entry	Benzylic compound	Product	yield(%)[a]
1	 **310**	 **315**	69
2	 **311**	 **316**	45
3	 **312**	 **317**	47
4	 **313**	 **318**	61
5	 **314**	 **319**	66

[a] *Yield of the isolated product.*

yields (Table 33, Entries 1-2,4-5). Cyclohexyl benzene underwent smooth transformation to 1-phenyl cyclohex-1-ene in moderate yield (Table 33, Entry 3). These transformations were completed within 15-17h at 60° C under atmospheric pressure of dioxygen and all the reactions yielded the tertiary alcohol **269** as the by product in quantitative yield (yield based on **268**). The allylic oxidation of alkenes is known to occur via metal-catalyzed autoxidation process, however, in the present case the reaction seems to be proceeding via a different pathway. We have observed that these reactions do not occur using catalytic amount of **268**, however, as we increase the quantity of **268**, then the allylic and benzylic oxidations proceed quite smoothly. Thus, in the oxidation of cyclohexene, increasing the quantity of **268** from 0.1 equivalent to 1 equivalent we see a considerable increase in the yields of **84** and **116**. Further, enhancement in the yield of **84** and **116** were also observed by using 2 equivalents of **268**.

It is interesting to note that during the oxidation of cyclohexene in the presence of two equivalents of **268**, the formation of enone **84** is more than **116**. When the oxidation of cyclohexene was carried out in the presence of radical trap, ie. *2,4,6-tritertiarybutylphenol*, no inhibition of product formation was observed. This observation also rules out the occurrence of this reaction via metal catalyzed autoxidation process.

6.2.5 EPR Study

EPR spectrum of **99c** was recorded in acetonitrile solvent at ambient temperature which gave a very weak signal whose g_{iso} was found to be 2.0124, whereas, in the presence of ethyl 2-oxocyclopentanecarboxylate, a strong signal whose g_{iso} was found to be 2.0187 (Fig. 3). The spectra were recorded at different time intervals, however, the g-values were found to be constant. This result indicates the formation of superoxocobalt(III) species from **268**, dioxygen

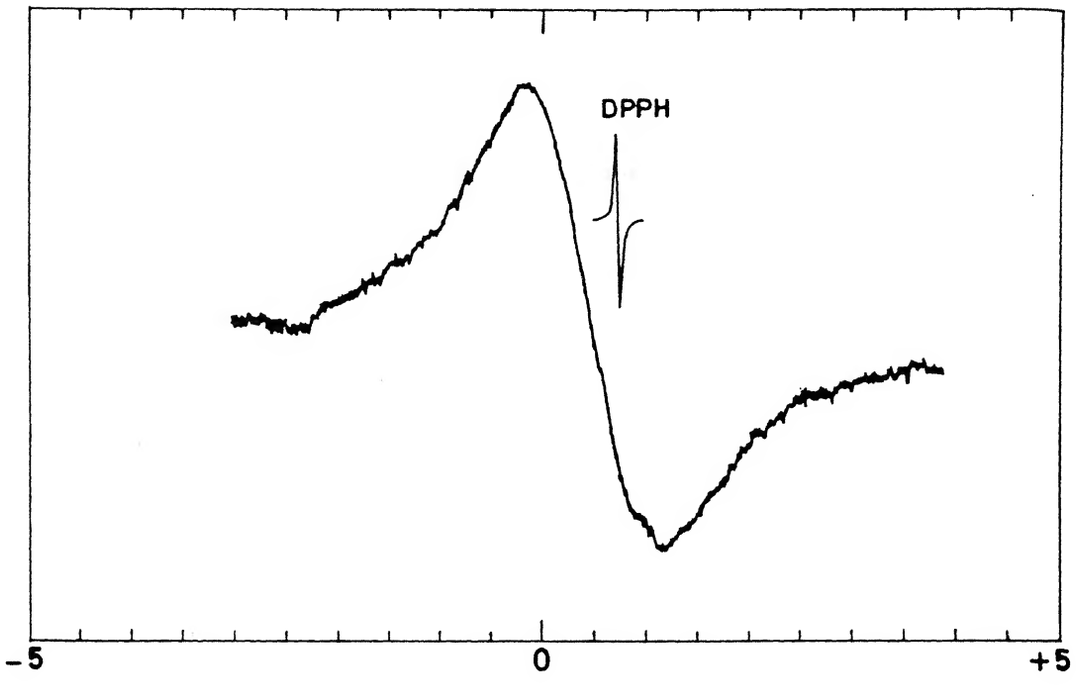


Fig. 3 EPR spectrum of **99c** in the presence of **268** and dioxygen

and catalyst **99c**. The formation of the superoxo species is only observed in the presence of **268** and this clearly indicates that the latter is helping the uptake of oxygen by catalyst, a similar observation has been reported by Basolo and coworkers[118] in related cobalt complexes.

Oxidation reaction of cyclohexene, in the presence of **99c** and dioxygen, was carried out using different carbonyl compounds whose EPR spectra were recorded at constant time and their g-values were found to be directly proportional to their product yields (Table 34, entries 1-4). The g-values and yields were correlated (Fig. 4), 2-methylpropanal **101** shows higher g-value and more yield whereas methyl isopropyl ketone **281** shows less g-value and does not react under this reaction conditions.

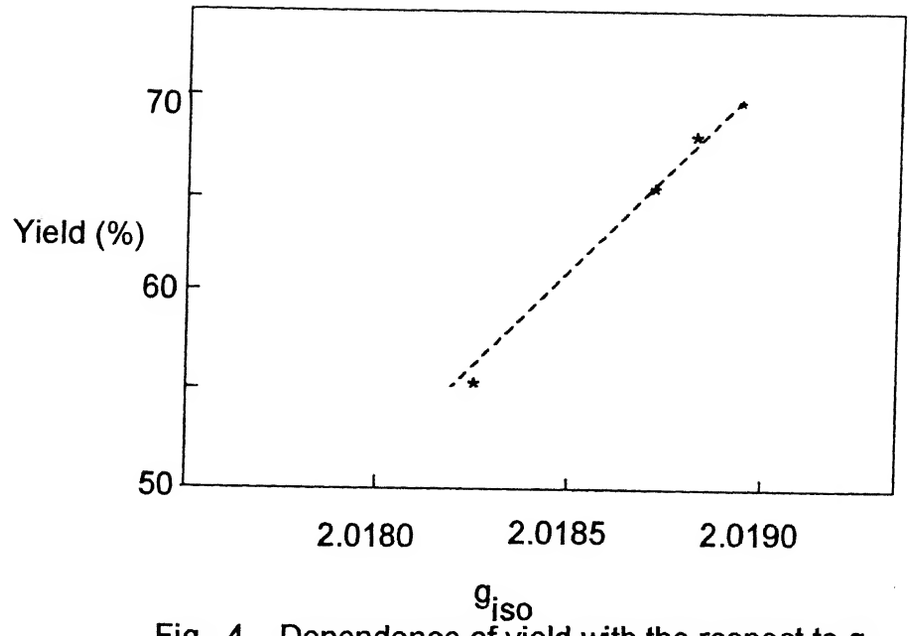
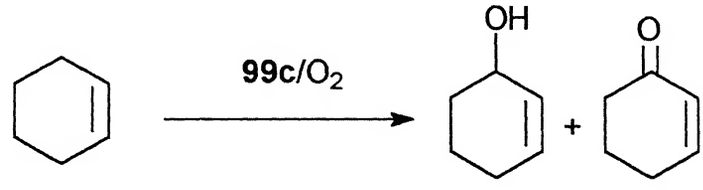
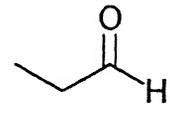
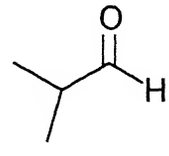
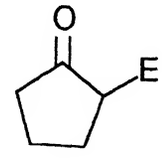
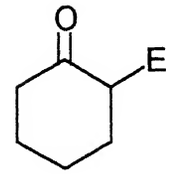


Fig. 4 Dependence of yield with the respect to g_{iso}

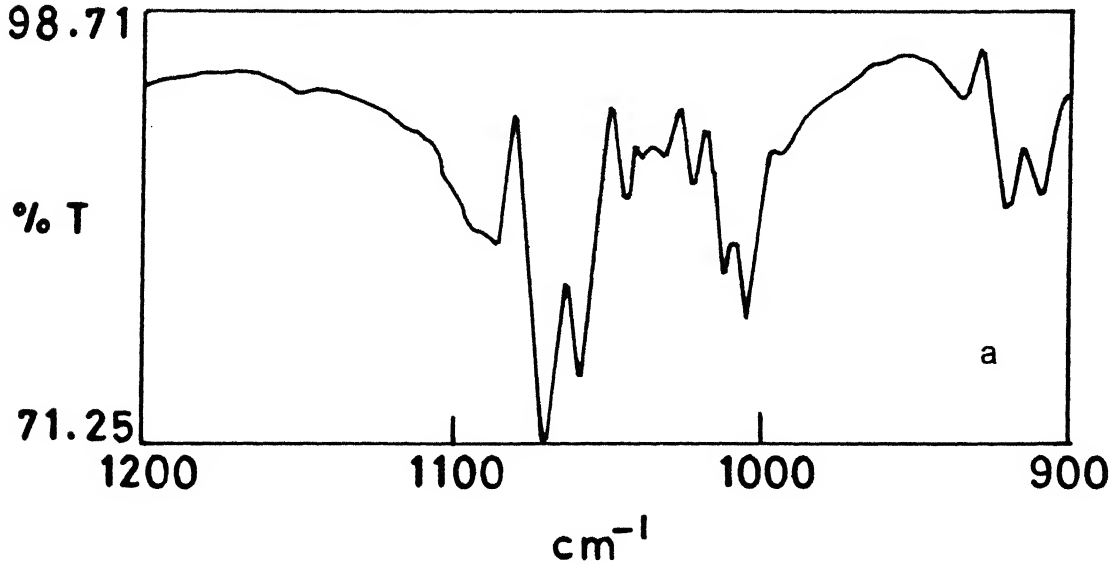
Table 34. Allylic Oxidation of Cyclohexene in the Presence of Dioxygen



Entry	Carbonyl Compound	g_{iso}	Yield(%)
1		1.0183	55%
2		1.0190	72%
3		1.0187	65%
4		1.0189	68%

6.2.6 IR Study

IR study of the reaction mixture having cyclopentanecarboxylate **268**, dioxygen and catalyst **99c** was carried out at different time interval. After three hours there was a strong



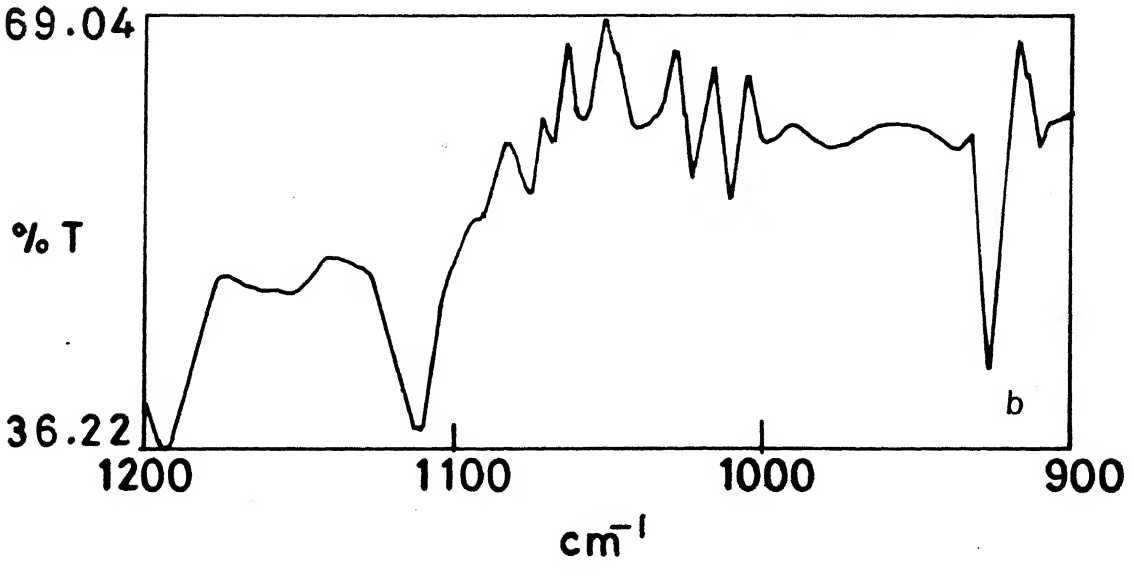
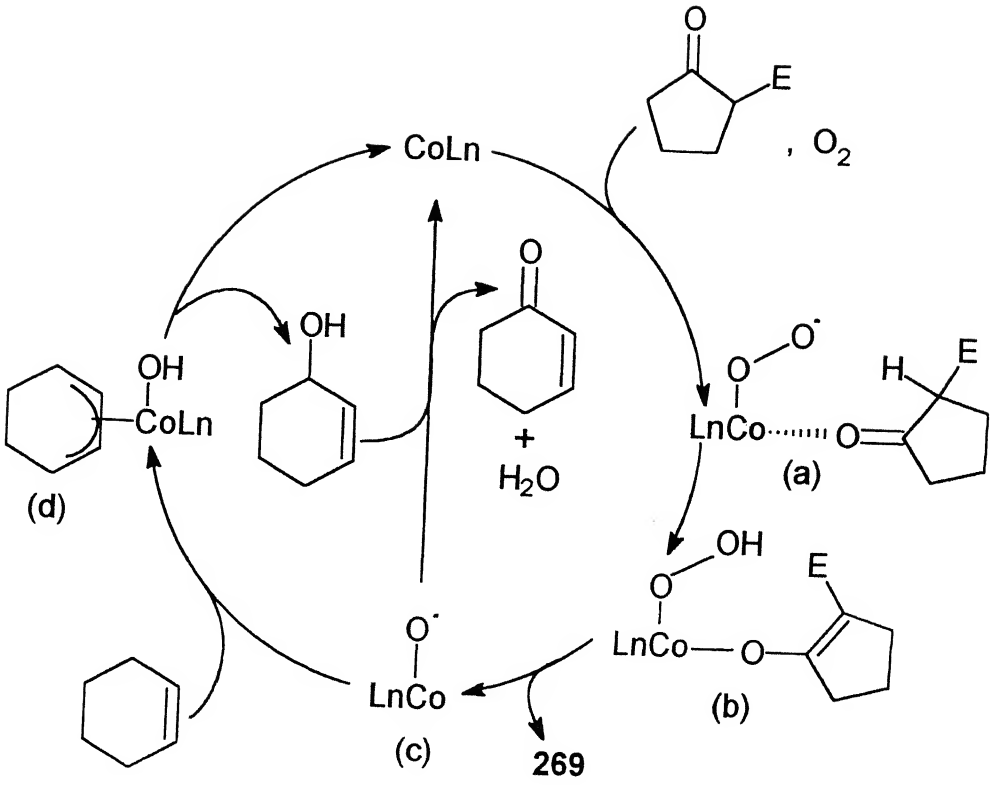


Fig. 5 (a) IR spectrum recorded at 0.25h. (b) IR spectrum recorded at 5h

absorption at 1193 cm^{-1}, which is a characteristic of O-O stretching of the superoxo complexes (Fig. 5)[119]. This was only observed in the presence of ethyl 2-oxocyclopentanecarboxylate and molecular oxygen. This clearly supports that the β-ketoester helps in the uptake of oxygen by the catalyst **99c**.

6.2.7 Mechanism

Catalytic cycle for this reaction may be initiated by the formation of (a) which may lead to the formation of cobalt enolate (b) via intramolecular hydrogen transfer. The rapid intramolecular hydroxylation of (b) will lead to **269** and the reactive cobalt oxo complex(c), which may abstract an allylic hydrogen atom to provide allylic alcohol via (d) and the complex **99c**. It is clear that the allylic alcohol is also prone to oxidation by (c) and thus, this would require more of the latter compound in order to achieve high conversion of alkene to the corresponding alcohol or enone. Due to this competitive reactions (i.e., allylic oxidation versus alcohol oxidation), more of (c) will be consumed which in turn would require more of **268** for high yield of conversion of alkenes to alcohol or ketone (Scheme 57) Thus, the dependence of **268** on the overall yield of this reaction may be understood if we invoke the formation of (c) as the reactive species. A species analogous to (c) has already been proposed by Kochi and coworkers during the cobalt catalyzed oxidation of alkenes with iodosylbenzene.[120] In light of this, the formation of can be understood by the rearrangement followed by the oxidation of the initially formed allylic radical from the corresponding alkenes. The conversion of cyclohexenone as presented in Scheme 56 gives an indication that this catalyst **99c** may be also useful for the oxidation of alcohol to ketone. The following section deals with studies on the oxidation of various alcohols with molecular oxygen in the presence of cobalt catalysts.



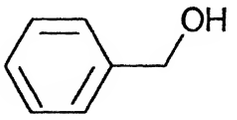
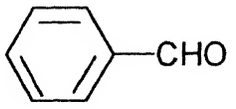
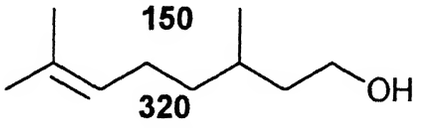
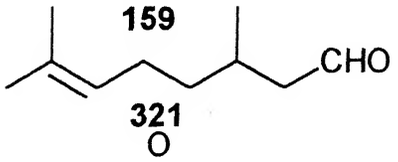
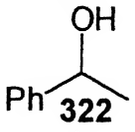
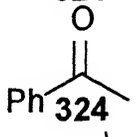
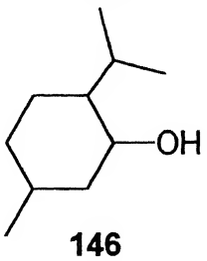
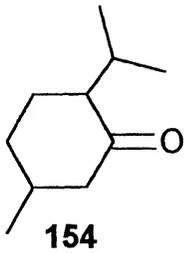
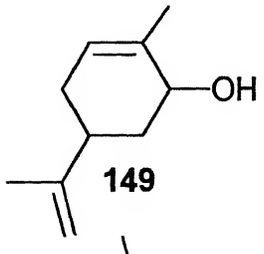
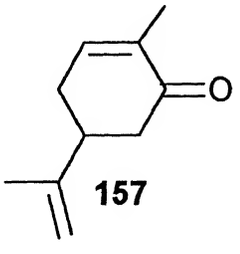
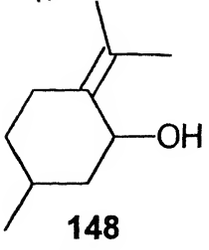
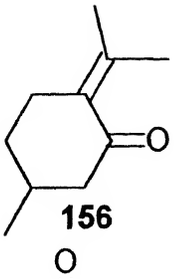
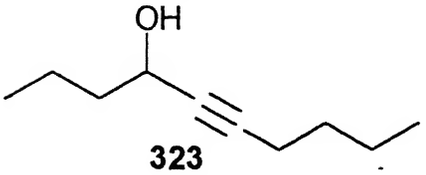
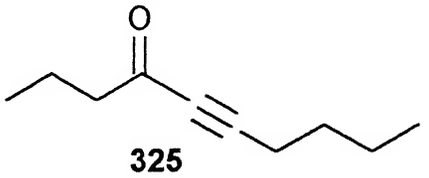
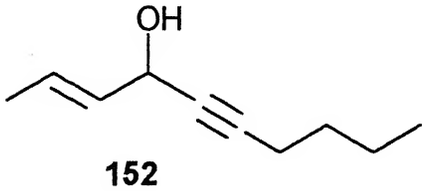
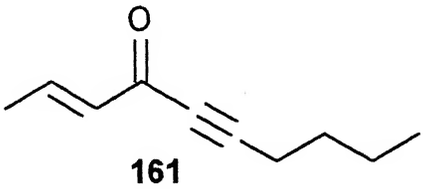
Scheme 57

6.2.8 Oxidation of Alcohols to Carbonyl Compounds

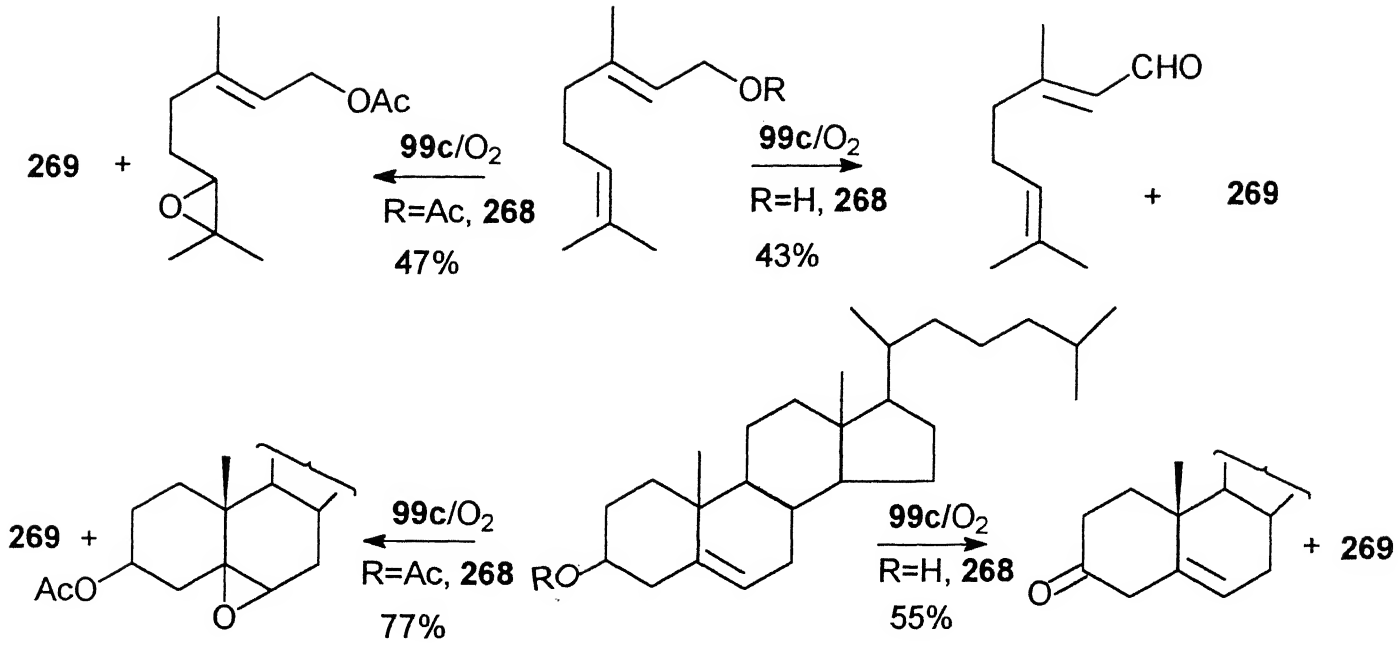
These reaction conditions are also suitable for the oxidation of primary and secondary alcohols to the corresponding carbonyl compounds. Thus, benzyl alcohol was selectively oxidized to the corresponding aldehyde in high yield (Table 35, Entry 1). Citronellol underwent smooth oxidation to citronellal in good yields (Table 35, Entry 3). 1-Phenylethanol, menthol, carveol and pugelol were selectively oxidized to the corresponding ketones in high yields (Table 35, Entries 5-8). Similarly, the enyne alcohols were smoothly oxidized to the corresponding ketones in good yield (Table 35, Entry 10 and 11). These transformations were carried out at ambient temperature, and requires longer reaction time for the completion of the reactions. However, at 50-60° C the reactions were completed within 10-12h. It is also noteworthy that the primary alcohols are oxidized slowly as compared with the secondary ones. Presence of molecular sieves 4A° facilitates the reaction as high conversion of alcohol to ketone is observed under these conditions. Interestingly, the olefinic alcohols can be selectively transformed to either the carbonyl compounds or epoxides under the experimental conditions. Thus, geraniol can be converted to citral by using equivalent amount of **268** and catalyst **99c** whereas geranyl acetate can be transformed to the corresponding epoxide in high yield (Scheme 58). A similar treatment on cholesterol provides cholestenone whereas cholesteryl acetate gives a mixture of epoxides in good yields (Scheme 58). The flexibility permitted by this transformation will be of great importance in achieving selective conversion of olefinic alcohols.

These reactions of may be proceeding via cobalt superoxo complex whose formation is facilitated by **268** which acts as a reductant. An EPR study of this reaction has indicated that the superoxide complex is formed only in the presence of **268** (Scheme 59). Hence, We believe that the cobalt(III) oxygen complex (a) may transform to the corresponding cobalt-enolate

Table 35. Cobalt(II) Catalysed Oxidation of Alcohols with Molecular Oxygen

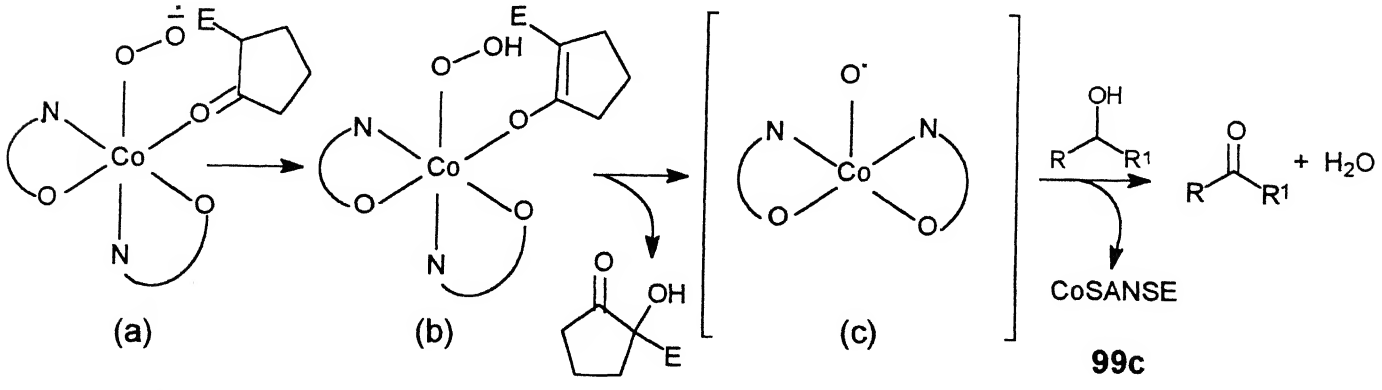
entry	alcohol	product	(yield %)[a]
1	 **150**	 **159**	(82)[b]
2	 **320**	 **321**	(49)
3	 **322**	 **324**	(85)[b]
4	 **146**	 **154**	(72)
5	 **149**	 **157**	(61)
6	 **148**	 **156**	(59)
7	 **323**	 **325**	(44)
8	 **152**	 **161**	(51)

[a]Isolated yields of the carbonyl compounds.[b]Yield determined by HPLC



Scheme 58

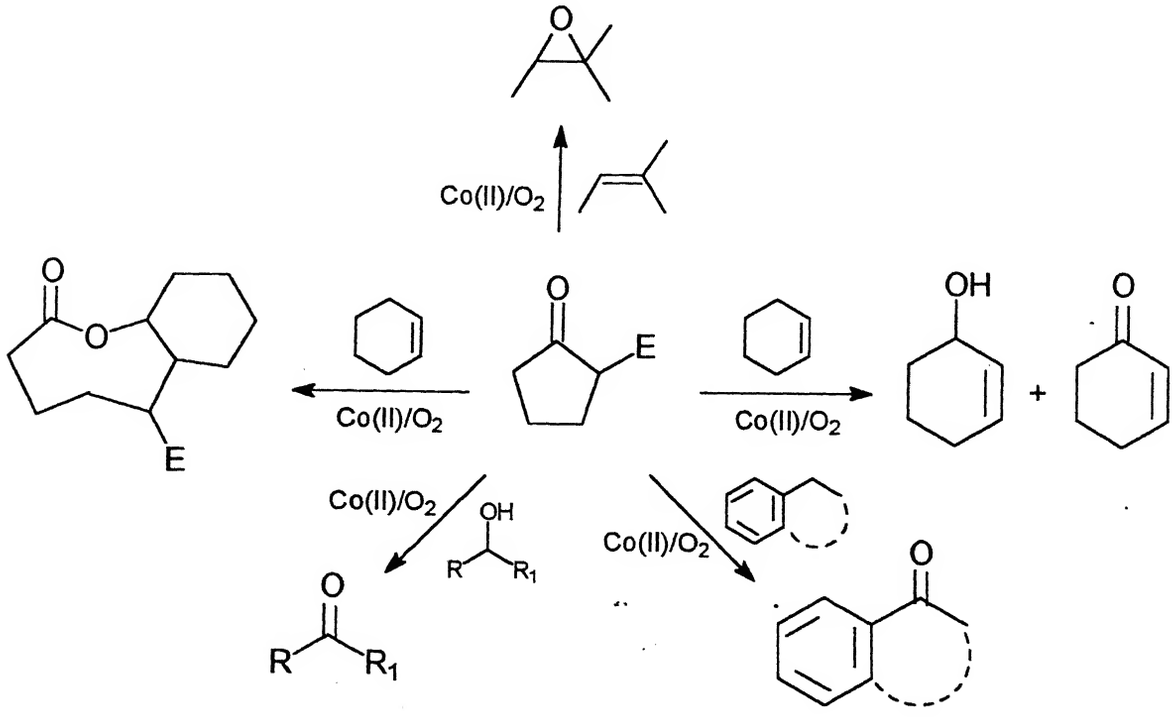
complex (b) via an intramolecular hydrogen abstraction. Rapid intramolecular hydroxylation of the cobalt enolate (b) will provide **269** and cobalt-oxo species (c) which may subsequently oxidize the alcohol to the corresponding carbonyl compounds and in the process the catalyst **99c** will be regenerated to complete the cycle.

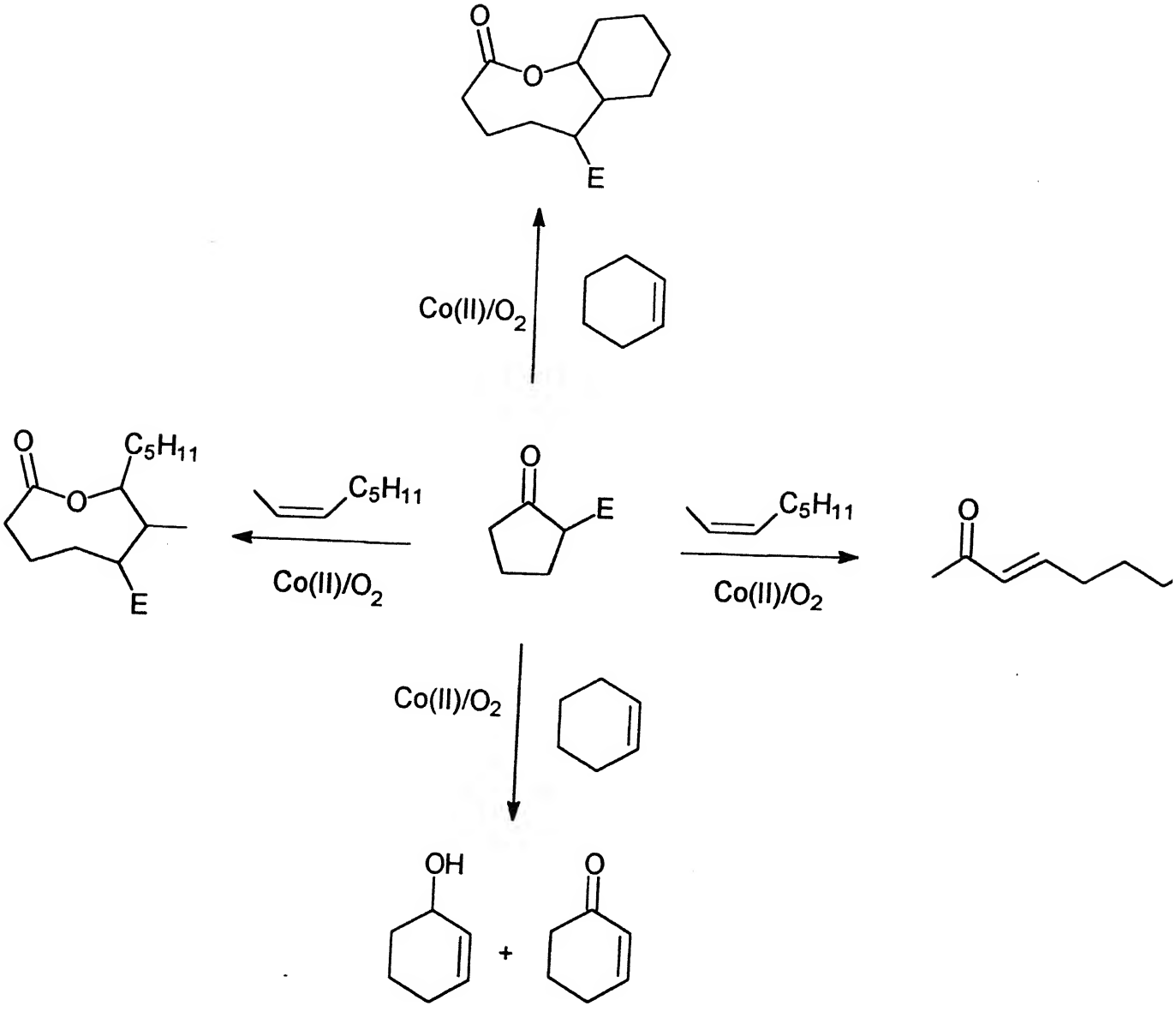


Scheme 59

6.2.9 Conclusion

In conclusion, this part provides a novel and efficient route to the generation of 1,3-dicarbonyl radicals which can be used for the synthesis of valuable oxygenated products such as macrocyclic lactones by oxidative addition with alkenes, selective epoxidation at the terminal trisubstituted double bonds, allylic, benzylic and alcohol oxidations. The reactivity of these chiral complexes is controlled by ligands is clearly evidenced in the lactone formation where catalyst **99a** mainly gives addition product whereas **99c** gives allylically oxidized product. These reactions are also substrate dependent as trisubtituted alkenes undergo epoxidation chemoselectively at the trisubstituted double bond whereas cyclic alkenes give allylically oxidized products. This methodology is also quite suitable for benzylic oxidations and selective oxidation of alcohols to carbonyl compounds. Finally, the thesis has been able to provide deep insight into the mechanistic rationale behind all the reactions by providing an evidence that these reactions proceeding via a common 1,3-dicarbonyl-cobalt intermediate. These observation are in conformity with the catalytic cycle proposed for these reactions.




O
O
E
Co(II)/O2
O
C5H11
O
E
C5H11
Co(II)/O2
O
E
C5H11
Co(II)/O2
O
Co(II)/O2
OH
O
+

6.2.10 Experimental

6.2.10.1 Materials. Sodium hydride was purchased from Fluka AG. Dimethyl carbonate and diethyl carbonate were obtained from Aldrich. Adipic acid was purchased from E. Merck(India) Ltd. These chemicals were purified prior to use according to the standard procedure.[121]

Cobalt(II) salophen (298).[122] Salicylaldehyde (1.22g, 5 mmol) and o-phenylenediamine (0.54g, 5 mmol) were stirred for 10 minutes and heated to become viscous. The mixture was allowed to stand for 20 minutes and poured into 50 ml of ethyl alcohol with vigorous stirring, the solid mass was filtered off with a Buchner funnel and dried at room temperature for 10h. The product, salophen ligand was obtained in 85% (0.8g) yield as yellow powder by recrystallization from ethyl alcohol.

mp. 165° C.

^{1}H NMR ($CDCl_3$): δ 6.6-7.5 (m, 12H), 8.5 (s, 2H), 13.0 (s, 2H).

The salophen ligand (0.97g, 5 mmol) and cobalt(II) acetate (1.3g, 5 mmol) was refluxed in 250ml methanol for 3h. The brown colored powder was filtered off with a Buchner funnel. The resulted complex was washed with methanol and ether, dried in vacuo at 80° C for 5h to give **298** (1.1g, 77%) as brown colored powder.

Preparation of [Bis(salicylidene-N-(Methyl 2-isopropylacetate)] cobalt (299). This complex **299** was prepared according to the procedure described for the preparation of **99d** in 75% yield as green colored crystals.

UV-Vis (CH_2Cl_2): λ_{max} 614, 629, 664 nm.

Conductivity: 25 mΩ cm^2 mol^{-1}.

IR (CH_3CN): υ_{max} 1730 cm^{-1}.

Anal. Calcd. for $C_{26}H_{32}O_6N_2Co$: C, 59.31; H, 6.08.

Found: C, 59.27; H, 6.10.

Preparation of Ethyl 2-oxocyclopentanecarboxylate (268). Granulated sodium (4.16g, 18 mmol) was prepared in a 250 ml round bottom flask. The sodium was covered with 75 ml of sodium dried benzene and the flask fitted with a reflux condenser protected from moisture by means of a calcium chloride guard tube. Diethyl adipate (25.25g, 125 mmol) was added in one lot followed by absolute ethyl alcohol (2 ml). The flask was warmed until a vigorous reaction set in and a cake of the sodium commenced to separate. The flask was continuously shaken by hand during the initial reaction. After the spontaneous reaction had subsided, the mixture was refluxed overnight and then cooled in ice. The product was decomposed in ice and dil. HCl (1:1). The acid was added until congo red paper turned blue. The benzene layer was separated and the aqueous layer was extracted with 50 ml benzene. The combined extracts were washed with $NaHCO_3$ solution (3 x 25 ml) and water (2 x 15 ml). Drying (Na_2SO_4) and removal of solvent in vacuo, provided a residue which was fractionated under reduced pressure. The product **268** (16.54g, 85%) was collected at 108-111° C/15 mm Hg.

^1H NMR (CCl_4): δ 1.25 (t, 3H, J=6.0 Hz), 1.7-2.5 (m, 6H), 2.9 (t, 1H, J=6.0 Hz), 4.2 (q, 2H, J=6.0 Hz).

IR (neat): υ_{max} 1755, 1730 cm^{-1}

Preparation of Methyl 2-oxocyclohexanecarboxylate (270). Sodium hydride (55-60% in oil, 0.46g, 20 mmol) was taken in a dry three necked 150 ml round bottom flask fitted with a water condenser and dropping funnel. The oil was removed using dry petroleum ether (3x10 ml) and the sodium hydride was covered with 10 ml of dry THF. To a stirred sodium hydride in THF, cyclohexanone (0.98g, 10 mmol) in 25 ml of dry THF was added dropwise under nitrogen atmosphere for 30 minutes at 0° C followed by the addition of dimethyl carbonate (1.08g, 12 mmol) in 30 ml of THF for 1h. Then, the reaction mixture was stirred at room temperature for 3h and quenched with ammonium chloride solution. Extracted with diethyl ether and brine (3x20 ml). Drying(Na_2SO_4) and removal of the solvent in vacuo, gave the crude compound which was distilled at 120° C/10 mm Hg to give **270** (1.25g, 80%) as colorless liquid.

^{1}H NMR (CCl_4): δ 1.3-1.9 (m, 6H), 2.2 (t, 2H), 3.2 (t, 1H, J=6.0 Hz), 3.6 (s, 3H).

IR(neat): υ_{max} 1730, 1715 cm^{-1}.

Preparation of Ethyl 2-oxocycloheptanecarboxylate (271). Prepared according to the above procedure and distilled at 128° C/10 mm Hg to afford **271** (1.42g, 10 mmol) as a liquid.

^{1}H NMR (CCl_4): δ 1.2 (t, 3H, J=6.0 Hz), 1.4-2.0 (m, 8H), 2.35 (t, 2H, J=6.0 Hz), 3.35 (t, 1H, J=6.0 Hz), 4.0 (q, 3H, J=6.0 Hz).

IR (neat): υ_{max} 1730, 1715 cm^{-1}.

6.2.10.2 General Procedure for the Synthesis of Lactones and Ketones

β-Ketoester (5 mmol), alkene (15 mmol) and cobalt(II) Schiff base complex **99a** (5 mol%) were stirred in dry acetonitrile at ambient temperature for 30-35h under dioxygen balloon. Solvent was removed in vacuo, and the residue was dissolved in ethyl acetate (35 ml).

The organic layer was successively washed with $NaHCO_3$ solution (3x25 ml), water (2x15 ml) and brine (2x15 ml). Drying(Na_2SO_4) and evaporation of the solvent gave the residue which was purified by column chromatography.

Compound 273. Ethyl 2-oxocyclopentanecarboxylate (0.78g,5 mmol), 1-hexene (1.26g,15 mmol) and cobalt(II) complex **99a** (5 mol%) were subjected to the above reaction conditions as described in the general procedure for 30h. Removal of the solvent and usual workup yielded the residue which was purified by column chromatography on silica gel (1:19 EtOAc/Pet. ether) to give **273** (0.51g, 40%) as a thick yellow liquid.

^1H NMR (CCl_4): δ 0.6-1.1 (m, 6H), 1.2-2.6 (m, 15H), 4.0 (q, 2H, J=6.0 Hz), 5.0-5.5 (m, 1H).

IR (neat): υ_{max} 1740, 1710 cm^{-1}.

MS (m/z): 238, 211, 183, 167, 165, 155, 141, 137, 127, 113, 112, 42.

Anal. Calcd. for $C_{14}H_{24}O_4$: C, 65.63; H, 9.38.

Found: C, 65.55; H, 9.39.

Compound 274. Ethyl 2-oxocyclopentanecarboxylate **268** (0.78g,5 mmol), Cyclohexene (1.23g, 15 mmol) and cobalt(II) complex **99a** (5 mol%) were stirred in acetonitrile at ambient temperature for 35h using dioxygen balloon. Usual workup and purification by column chromatography (silica gel 60-120 mesh; 1:19 EtOAc/Petroleum ether) afforded **274** (0.44g, 35%) as a thick yellow liquid.

^1H NMR (CCl_4): δ 0.9 (t, 3H, J=6.0 Hz), 1.5-2.5 (m, 16H), 4.0 (q, 2H, J=6.0 Hz), 5.0-5.8 (m, 1H).

IR (neat): υ_{max} 1735, 1710 cm^{-1}.

MS (m/z): 235, 162, 156, 114, 113, 112, 110, 100, 81, 42.

Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.14; H, 8.66.

Found: C, 66.10; H, 8.69.

Compound 275. Ethyl 2-oxocyclopentanecarboxylate (0.78g,5 mmol), 4-acetoxy hex-1-ene (1.42g, 10 mmol) and cobalt(II) acetate (1.33g, 7.5 mmol) were stirred at 70° C for 15h in acetic acid under oxygen atmosphere. The reaction mixture was mixed with sodium bicarbonate solution (pH=7) and extracted with ethyl acetate. The organic layer was successively washed with sodium bicarbonate solution (2x15 ml), water (2x10 ml) and brine (2x15 ml). Evaporation of the solvent gave the residue which was on column chromatography purification yielded **275** (0.625g, 40%) as yellow oil.

^{1}H NMR (CCl_4): δ 0.7-1.1 (m, 6H), 1.2-2.5 (m, 16H), 4.0 (q, 2H, J=6.0Hz), 4.5-5.2 (m, 2H).

IR (neat): υ_{max} 1710, 1735 cm^{-1}.

MS (m/z): 241, 199, 182, 156, 142, 126, 98, 83, 44.

Anal. Calcd. for $C_{16}H_{26}O_6$: C, 61.15; H, 8.23.

Found: C, 61.11; H, 8.25.

Compound 276. Methyl 2-oxocyclohexanecarboxylate **270** (0.78g, 5 mmol), 1-hexene (1.26g, 15 mmol) and cobalt(II) complex **99a** (5 mol%) under the reaction conditions described for **274** provided **276** (0.54g, 42%) as yellow colored oil.

^{1}H NMR (CCl_4): δ 1.0 (t, 3H, J=6.0 Hz), 1.1-2.5 (m, 17H), 3.6 (s, 3H), 5.0-5.6 (m, 1H).

IR (neat): υ_{max} 1735, 1710 cm^{-1}.

Anal. Calcd. for $C_{14}H_{24}O_4$: C, 65.63; H, 9.38.

Found: C, 65.66; H, 9.42.

Compound 279. Ethyl 2-oxocycloheptanecarboxylate **271** (0.92g, 5 mmol), 1-hexene (1.26g, 15 mmol) and cobalt(II) acetate (1.33g, 7.5 mmol) were reacted according to the reaction conditions mentioned for the synthesis of **275** for 15h to give **279** (0.36g, 27%) as yellow colored oil on column chromatography.

^{1}H NMR (CCl_4): δ 0.7-1.1 (m, 6H), 1.5-2.5 (m, 20H), 4.0 (q, 2H, J=6.0 Hz).

IR (CCl_4): υ_{max} 1735, 1710 cm^{-1}.

MS (m/z): 269(M^{+1}), 268(M^+)

Anal Calcd. for $C_{16}H_{28}O_3$: C, 71.64; H, 10.45.

Found: C, 71.56; H, 10.48

Compound 280. Ethyl 2-oxocyclopentanecarboxylate (0.78g, 5 mmol), (Z)-2-octene (1.12g, 10 mmol) and cobalt(II) complex **99a** (5 mol%) under the reaction conditions described for **273** provided **280** (0.45g, 32%) yield as yellow colored liquid.

^{1}H NMR (CCl_4): δ 0.7-1.1 (m, 6H), 1.5-2.5 (m, 19H), 4.0 (q, 2H, J=6.0 Hz), 5.0-5.8 (m, 1H).

IR (neat): υ_{max} 1735, 1710 cm^{-1}.

Anal. Calcd. for $C_{16}H_{28}O_4$: C, 67.60; H, 9.86.

Found: C, 67.56; H, 9.88

Preparation of Methyl 3-acetoxy-5,9-dimethyl-deca-4,8-dienoate(285).

Zinc dust (previously dried at 100° C, 0.4g, 6.1 mmol) was taken in a 100 ml dry three necked round bottom flask which was equipped with a 50 ml separating funnel and condenser (inserted with calcium chloride guard tube) on a stirrer. A solution of methyl bromoacetate (0.77g, 5 mmol) and citral (0.93g, 6.1 mmol) in dry benzene (16 ml) and dry diethyl ether (4 ml) were taken in the separating funnel. The solution (about ~5 ml) was added to the zinc and warmed

the flask gently until the reaction started. The mixture was stirred and the remaining solution was added dropwise at such a rate that moderate refluxing occurred (about 1h). The reaction mixture was refluxed for further 30 minutes. The flask was then cooled in ice bath, and 2 ml of cold 10% H_2SO_4 was added with vigorous stirring. The benzene layer was exracted and washed with 5% H_2SO_4, 10% Na_2CO_3 solution (2x20 ml) and water(2x15 ml). Drying(Na_2SO_4) and removal of the solvent gave a residue, which was purified on column chromatography (on silica gel 60-120 mesh, 1:19 EtOAc/Petroleum ether) to afford the hydroxy ester and this was acylated with acetic anhydride, triethylamine and catalytic amount of DMAP to give **285** (1.04g, 67%) as a liquid.

^{1}H NMR ($CDCl_3$): δ 1.6 (s, 3H), 1.7-1.9 (m, 9H), 2.1-2.4 (m, 6H), 3.7 (s, 3H), 5.1-5.4 (m, 1H), 5.7-6.0 (m, 2H).

IR (neat): υ_{max} 1735 cm^{-1}.

Preparation of 4-acetoxy-6,10-dimethyl-undec-1,5,9-triene (286).

Zinc (1.11g, 17 mmol) was added to a solution of citral (1.9g, 12.5 mmol) and allyl bromide (1.2g, 10 mmol) in DMF (20 ml) and stirred at ambient temperature for 1h. The exothermic reaction was completed within 45 minutes. The reaction mixture was quenched with saturated NH_4Cl solution (50 ml) and extracted with ethyl acetate (2x25 ml). The combined ethyl acetate layer was successively washed with water (5x25 ml) and brine (2x15 ml). Drying (Na_2SO_4) and evaporation of the solvent in vacuo afforded the residue which was purified by column chromatography, followed by acylation afforded **286** (1.58g, 67%) as a liquid.

^{1}H NMR ($CDCl_3$): δ 1.5-1.8 (m, 9H), 1.9 (s, 3H), 2.0-2.3 (m, 6H), 4.7-5.2 (m, 4H), 5.2-5.9 (m, 2H).

IR (neat): υ_{max} 1735 cm^{-1}.

1-(Trimethylsilyloxy)cyclohexene(288). Chlorotrimethylsilane (2.16g,20 mmol) was slowly added to a stirred solution of anhydrous sodium bromide (2.04g, 20 mmol) in dry DMF (50 ml) over a period of 10 minutes. The mixture was stirred at room temperature for 20 minutes, and during this period sodium chloride was precipitated. At this stage cyclohexanone (1.22g, 12.5 mmol) was added. After 20 minutes triethylamine (2.0g, 20 mmol) was added and the resulting mixture was stirred under nitrogen at room temperature for 4h. Extracted with petroleum ether (3x20 ml) and washed with saturated $NaHCO_3$ solution (2x20 ml). Then, the organic layer was washed with water (2x15 ml). Drying (Na_2SO_4) and evaporation of the solvent yielded the crude compound which was purified on column chromatography to obtain **288** (3.06g, 90%) as a liquid.

^1H NMR (CCl_4):δ 0.0 (s, 9H), 1.3-1.6(m, 4H), 1.7-2.0(m, 4H), 4.6 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 1664 cm^{-1}.

6.2.10.3 General Procedure for the Synthesis of Epoxides. Aldehyde (10 mmol) and unactivated alkene (5 mmol) were added to a stirred solution of cobalt(II) Schiff base complex (~20 mg) in acetonitrile. The reaction was carried out at ambient temperature under dioxygen balloon for 20-24h. The solvent was evaporated in vacuo, and the residue was dissolved in diethyl ether. The usual workup followed by column chromatography purification afforded the epoxides in good yields.

Methyl3-acetoxy-5,9-dimethyl-8,9-epoxydecanoate (290). Methyl 3-acetoxy-5,9-dimethyl deca-8-enoate (0.68g,2.5 mmol), methyl 2-oxocyclopentanecarboxylate (0.78g,5 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the reaction conditions as described in the general procedure to give **290** (0.22g, 32%) as a clear, yellow oil.

^{1}H NMR ($CDCl_3$): δ 0.8 (d, 3H, J=6.5 Hz), 1.1 (s, 6H), 1.2-1.6 (m, 7H), 1.9 (s, 3H), 2.1 (d, 2H, J=6.0 Hz), 2.6 (t, 1H, J=6.0 Hz), 3.7 (s, 3H), 4.6-4.9 (m, 1H).

IR (neat): υ_{max} 1735, 1375, 1250 cm^{-1}.

Anal. Calcd. for $C_{15}H_{26}O_5$: C, 62.93; H, 9.09.

Found: C, 62.90; H, 9.14.

4-Acetoxy-6,10-dimethyl-9,10-epoxyundec-1-ene (291). 4-Acetoxy-6,10-dimethyl undeca-1,9-diene (0.6g, 2.5 mmol) and methyl 2-oxocyclopentanecarboxylate (0.78g, 5 mmol) and cobalt(II) complex **99c** (5 mol%) under the above reaction conditions gave **291** (0.18g, 29%) as a clear, yellow oil.

^{1}H NMR (CCl_4): δ 0.9 (d, 3H, J=6.0 Hz), 1.1 (s, 6H), 1.2-1.8 (m, 7H), 1.9 (s, 3H), 2.0-2.3 (m, 2H), 2.6 (t, 1H, J=6.0 Hz), 4.7-5.1 (m, 3H), 5.2-5.7 (m, 1H).

IR (neat): υ_{max} 1720, 1375, 1250 cm^{-1}.

Anal. Calcd. for $C_{15}H_{26}O_3$: C, 70.86; H, 10.24.

Found: C, 70.82; H, 10.25.

Methyl 3-acetoxy-5,9-dimethyl-8,9-epoxydeca-4-enoate (292). Methyl 3-acetoxy-5,9-dimethyl deca-4,8-dienoate (0.67g, 2.5 mmol), methyl 2-oxocyclopentanecarboxylate (0.78g, 5 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the reaction conditions as described in the general procedure to give **292** (0.21g, 28%) as a clear, yellow oil.

^{1}H NMR ($CDCl_3$): δ 1.2 (s, 6H), 1.6 (s, 3H), 1.7-1.9 (m, 2H), 2.0 (s, 3H), 2.05-2.3 (m, 4H), 2.6 (t, 1H, J=6.0 Hz), 3.7 (s, 3H), 5.1-5.4 (m, 1H), 5.7-6.0 (m. 1H).

IR (neat): υ_{max} 1735, 1375, 1250 cm^{-1}.

Anal. Calcd. for $C_{15}H_{24}O_5$: C, 63.38; H, 8.45.

Found: C, 63.45; H, 8.48.

4-Acetoxy-6,10-dimethyl-9,10-epoxyundeca-1,5-diene (293). 4-Acetoxy-6,10-dimethyl undeca-1,5,9-triene (0.59g, 2.5 mmol) and methyl 2-oxocyclopentanecarboxylate (0.78g, 5 mmol) were reacted in the presence of cobalt(II) compelx **99c** (5 mol%) were subjected to the above reaction conditions for 35h to give **293** (0.18g, 28%) as a clear, yellow oil.

^{1}H NMR (CCl_4): δ 1.1 (s, 6H), 1.2-1.8 (m, 5H), 1.9 (s, 3H), 2.0-2.3 (m, 4H), 2.7 (t, 1H, J=6.0 Hz), 4.7-5.0 (m, 3H), 5.0-5.7 (m, 2H).

IR (neat): υ_{max} 1720, 1375, 1250 cm^{-1}.

Anal. Calcd. for $C_{15}H_{24}O_3$: C, 71.43; H, 9.52.

Found: C, 71.40; H, 9.54.

2-Hydroxycyclohexanone (295). 1-(Trimethylsilyloxy)cyclohexene (0.85g, 5 mmol), methyl 2-oxocyclopentanecarboxylate (1.56g, 10 mmol) and cobalt(II) complex **99c** (5 mol%) under the above reaction conditions gave **295** (0.87g, 70%) as liquid.

^{1}H NMR (CCl_4): δ 1.2-1.8 (m, 6H), 2.2 (t, 2H, J=6.0 Hz), 4.4 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 3450, 1710 cm^{-1}.

Preparation of Methyl 2-Methylacetoacetate (296). An oven dried three necked round bottom flask equipped with dropping funnel and condenser was flushed with nitrogen. Sodium hydride (0.46g, 20 mmol) (55-60 % in oily suspension was washed thrice with dry petroleum ether prior to use), mixed with 50 ml of freshly distilled THF was taken in this three necked flask. The flask was cooled to 0° and methyl acetoacetate (1.16g, 10 mmol) in 10 ml of dry THF was added dropwise through dropping funnel. Formation of anion in the reaction indicated by

evolution of hydrogen gas in the reaction mixture. The mixture was stirred over a period of 30 minutes. Methyliodide (1.55g, 11 mmol) in 15 ml of THF was added dropwise over a period of 30 minutes. The reaction mixture was allowed to stir at ambient temperature for a period 3h. The reaction mixture was quenched with saturated NH_4Cl solution and extracted with diethyl ether (3x15 ml). The organic layer was successively washed with saturated $NaHCO_3$ solution (2x10 ml) and brine (2x10 ml). Drying (Na_2SO_4) and evaporation of solvent in vacuo, gave the crude compound which was purified by column chromatography to give **296** (1.1g, 85%) as a liquid.

^1H NMR(CCl_4): δ 1.1 (d, 3H, J=6.0 Hz), 2.1 (s, 3H), 3.3 (q, 1H, J=6.0 Hz), 3.6 (s, 3H).

IR (neat): υ_{max} 1730, 1720 cm^{-1}.

6.2.10.4 General procedure for Allylic Oxidation. Alkene (5 mmol), β-ketoester (10 mmol) and cobalt(II) Schiff base complex (5 mol%) were stirred at ambient temperature for 30-35h using dioxygen balloon in acetonitrile. The solvent was removed in vacuo, and the residue was dissolved in diethyl ether. The ether layer was washed with $NaHCO_3$ solution (4 x 25 ml), water (2x15 ml) and brine (2 x 20 ml). Drying(Na_2SO_4) and evaporation of the solvent in vacuo, provided the residue which was distilled or purified by column chromatography on silica gel (60-120 mesh).

2,2,5-Trimethyl2,4-heptadienone (304). Δ^3-Carene (0.68g, 5 mmol), ethyl 2-oxocyclopentane-carboxylate (1.56g, 10 mmol) and cobalt(II) complex **99c** (5 mol%) were subjected to the reaction conditions described in the general procedure for 35h to afford **304** (0.50g, 67%) as a liquid on column chromatography (silca gel 60-120 mesh; 1:19 EtOAc/Pet. ether).

^1H NMR(CCl_4): δ 1.1 (s, 6H), 2.0 (s, 3H), 2.6 (s, 2H), 5.7-6.1 (m, 3H).

UV-Vis (MeOH): 267 nm.

IR (neat): υ_{max} 1690, 1630 cm^{-1}.

Anal. Calcd. for $C_{10}H_{14}O$: C, 80.00; H, 9.33.

Found: C, 79.97; H, 9.38

p-Cymene (306). Phellandrene (0.68g, 5 mmol), ethyl 2-oxocylopentanecarboxylate (1.56g, 10 mmol) and cobalt(II) complex **99c** (5 mol%) under the above reaction conditions afforded **306** (0.48g, 71%) as a clear liquid on distillation. This compound was also compared with authentic by gas chromatography.

^1H NMR (CCl_4): δ 1.2 (d, 6H, J=6.0 Hz), 2.2 (s, 3H), 2.5-3.0 (m, 1H), 6.9 (s, 4H).

bp.: 179° C.

(E)-4-Oxooct-2-ene (307). (Z)-2-Octene (0.56g, 5 mmol) , ethyl 2-oxocylopentanecarboxylate (1.56g, 10 mmol) and cobalt(II) complex (5 mol%) were subjected to the above reaction conditions for 35h to yield **307** (0.34g, 54%) as a liquid.

^1H NMR(CCl_4): δ 0.75 (t, 3H, J=6.0 Hz), 1.0-1.7 (m, 4H), 2.0 (s, 3H), 1.8-2.3 (m, 2H), 5.85 (d, 1H, J=14.0 Hz), 6.2-6.9 (m, 1H)

IR (neat): υ_{max} 1720 cm^{-1}.

UV-Vis(MeOH): λ_{max} 228 nm.

Anal. Calcd. for $C_8H_{14}O$: C, 76.19; H, 11.11.

Found: C, 76.00; H, 11.14.

6.2.10.5 General Procedure for Benzylic oxidations. Benzylic compound (5 mmol), ethyl 2-oxocyclopentanecarboxylate (15 mmol) and cobalt(II) complex **99c** were stirred at 60-65° C

Preparation of Secondary Alcohols. Alcohols were purchased or prepared by $NaBH_4$ reduction and purified prior to use by distillation or crystallization.

7-Hydroxydeca-5-yne (323). This compound was prepared according to the procedure described for the preparation of **152** from crotonaldehyde and 1-hexyne.

^1H NMR ($CDCl_3$): δ 0.6-1.0 (m, 6H), 1.1-1.9 (m, 8H), 2.2 (t, 2H, J=7 Hz), 3.5 (s, 1H), 4.3 (t, 1H, J=7.0 Hz).

IR (neat): υ_{max} 3450 cm^{-1}.

6.2.10.6 General Procedure for the Oxidation of Secondary Alcohols to Carbonyl Compounds.

Alcohol (5 mmol), ethyl 2-oxocylopentanecarboxylate (10 mmol) and cobalt(II) Schiff base complex **99a** (5 mol%) were stirred at 60-65°C for 10-15h using dioxygen balloon in acetonitrile solvent. The removal of the solvent and usual work up by ethyl acetate afforded the residue which was purified on column chromatography or performed on HPLC/gas chromatography.

Citronellal (321). Citronellol (0.39g, 2.5 mmol), ethyl 2-oxocylopentanecarboxylate (0.78g, 5 mmol) and cobalt(II) complex **99c** (5 mol%) were stirred at 60° C as described in the general procedure for 12h to give **321** (0.16g, 42%) on column chromatography.

^1H NMR (CCl_4): δ 0.9 (d, 3H, J=6.0Hz), 1.1-1.4 (m, 3H), 1.6 (s, 6H), 1.9-2.2 (m, 4H), 5.1 (t, 1H, J=6 Hz), 9.6 (t, 1H, J=2.0 Hz).

IR (neat): υ_{max} 1720 cm^{-1}.

7-Oxodeca-5-yne (325). Reaction of 7-Hydroxy deca-5-yne (0.77g, 5 mmol) with ethyl 2-oxocyclopentanecarboxylate (1.56g, 10 mmol) in the presence of cobalt(II) complex **99c** (5 mol%) under the above reaction conditions afforded **325** (0.33g, 44%) as a liquid on column chromatography.

^1H NMR ($CDCl_3$): δ 0.6-1.0(m, 6H), 1.1-1.9(m, 6H), 2.1-2.3(m, 4H).

IR (neat): υ_{max} 2200, 1730 cm^{-1}.

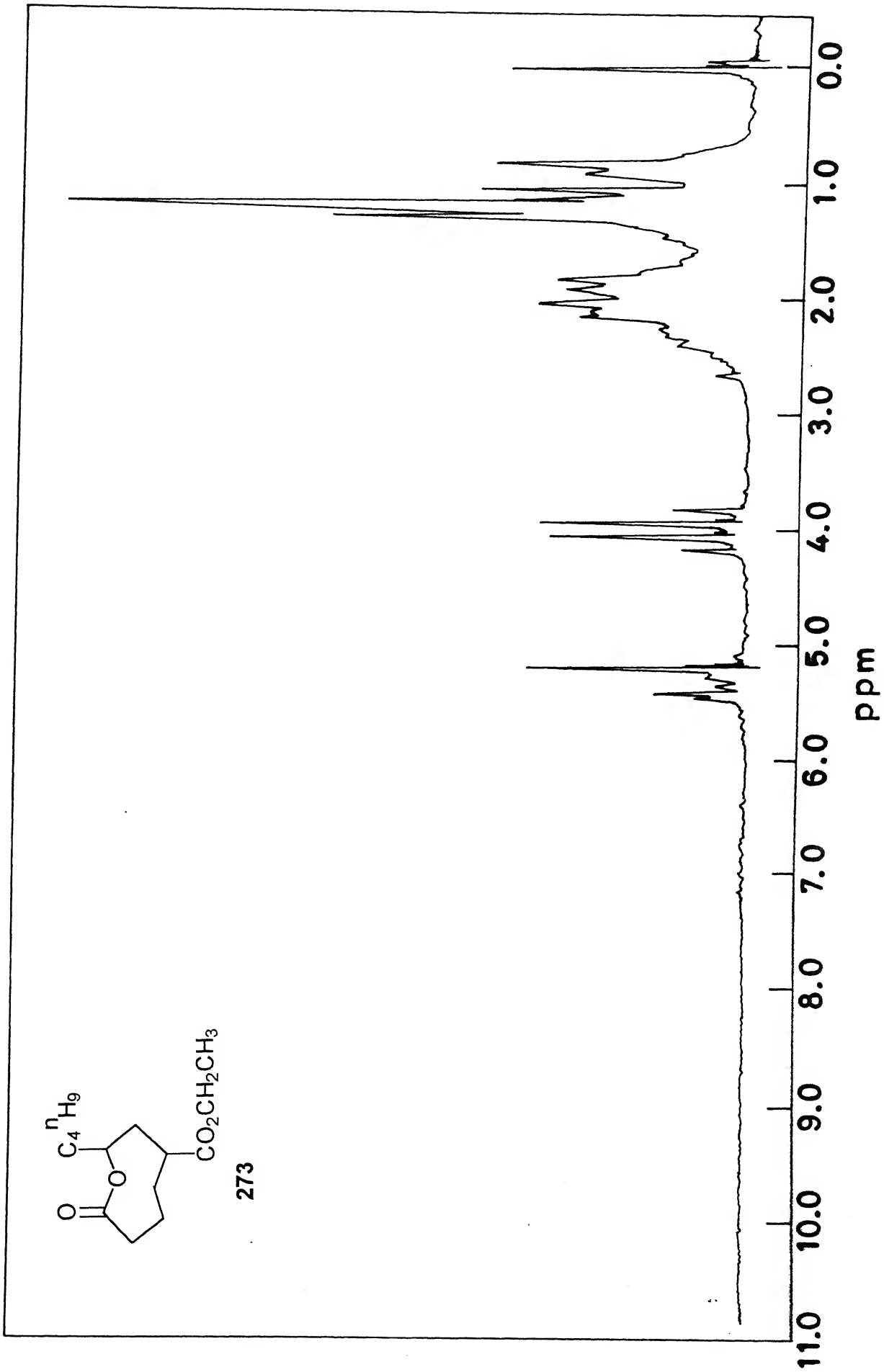
Anal. Calcd. for $C_{10}H_{16}O$: C, 78.94; H, 10.52.

Found: C, 78.89; H, 10.59.

Citral (326). Geraniol (0.77g, 5 mmol), ethyl 2-oxocyclopentanecarboxylate (0.78g, 10 mmol) and cobalt(II) complex **99c** were subjected to the above reaction conditions to give **326** (0.16g, 44%) as a liquid on column chromatography.

^1H NMR (CCl_4): δ 1.65 (s, 6H), 1.9-2.2(m, 7H), 4.7-5.1(m, 2H), 9.6 (t, 1H, J=6.0 Hz).

IR (neat): υ_{max} 1720 cm^{-1}.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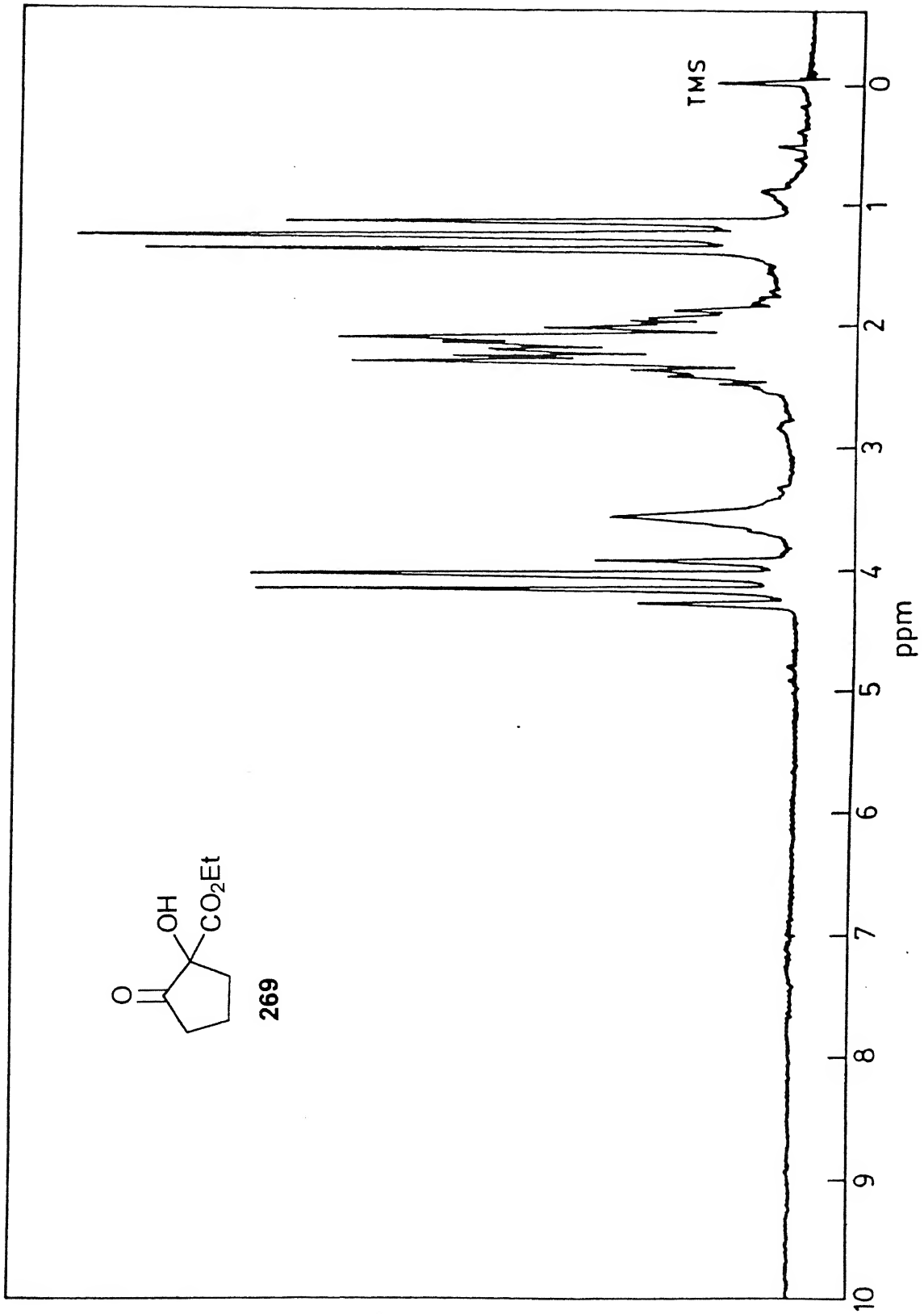

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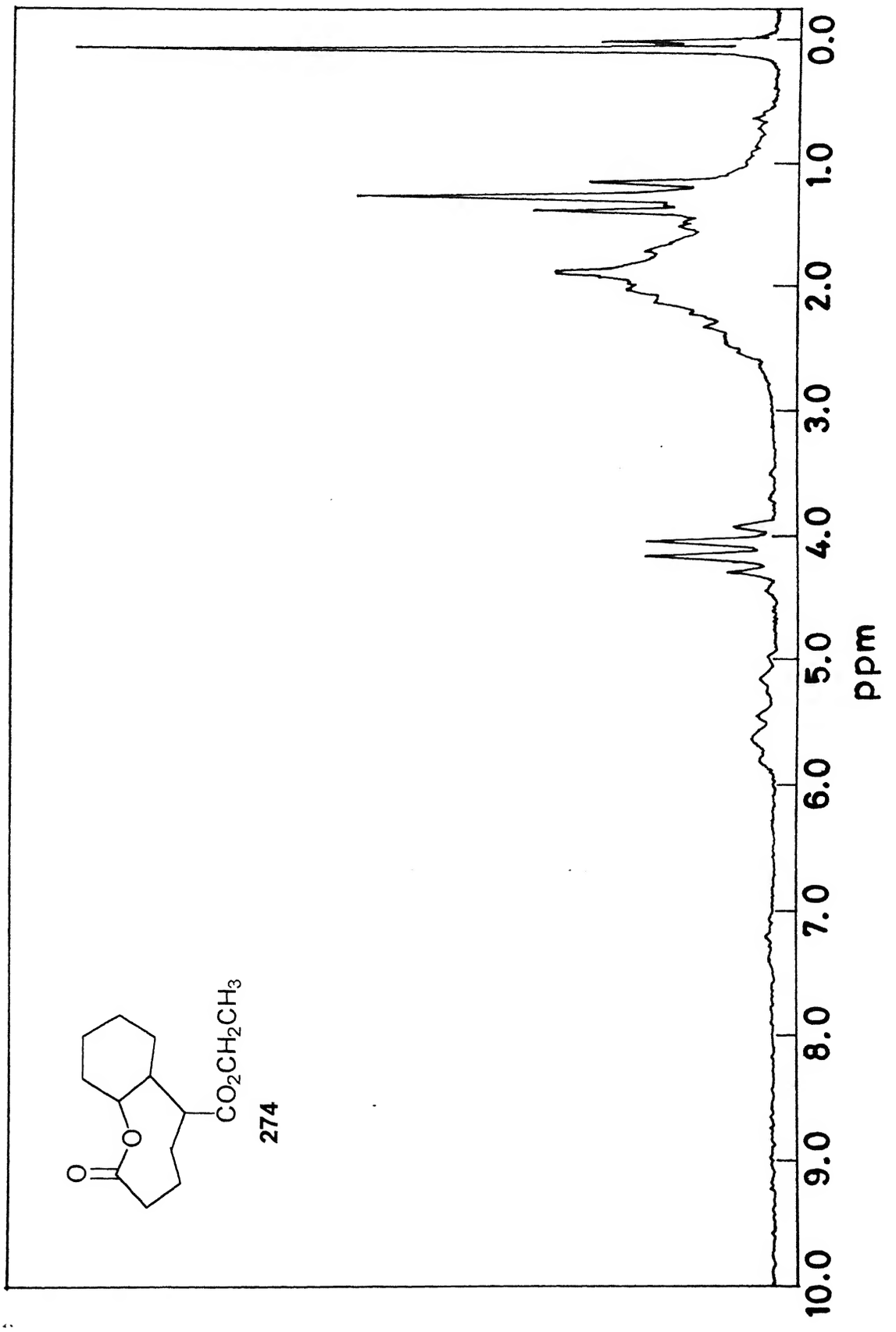

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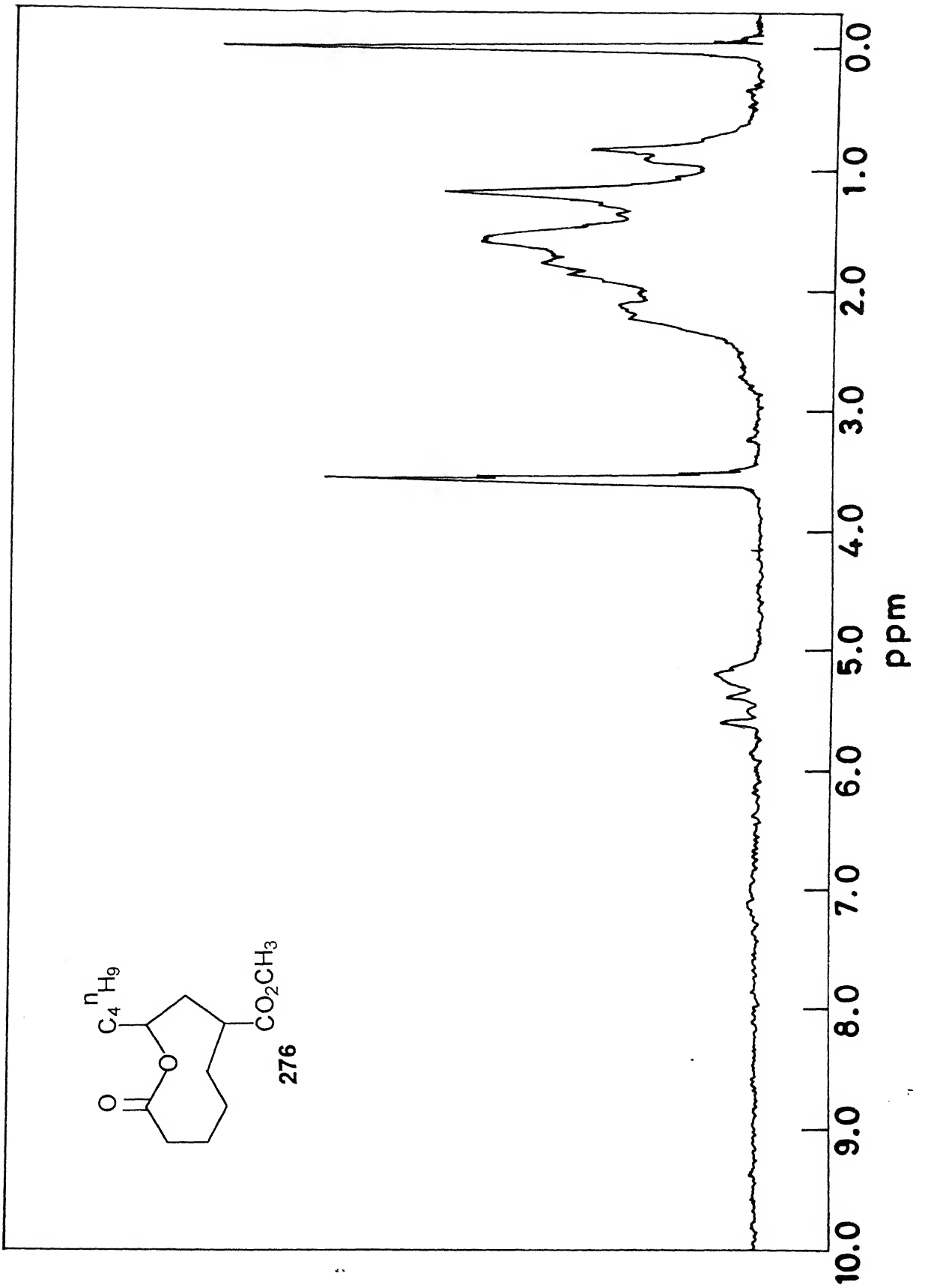

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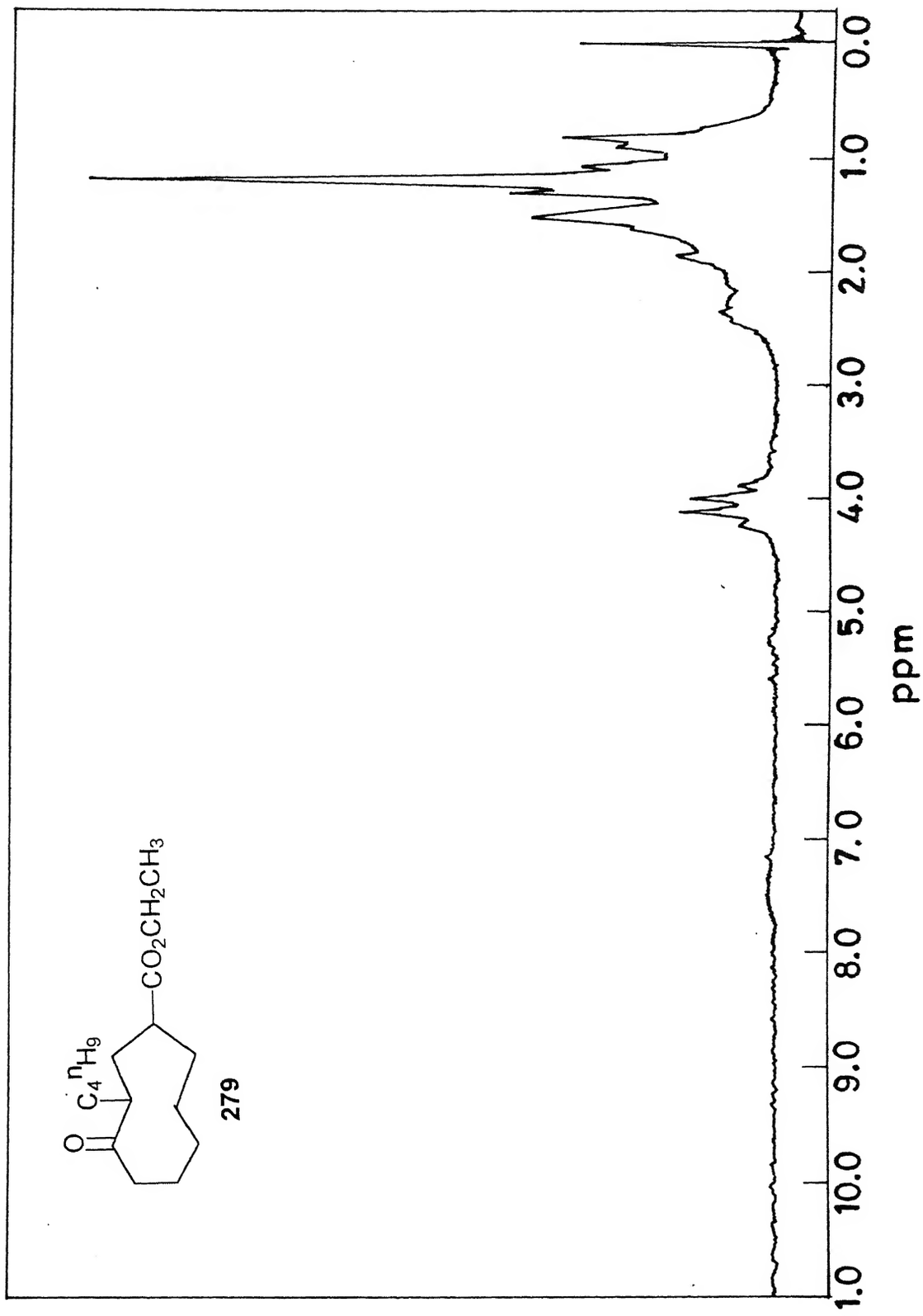
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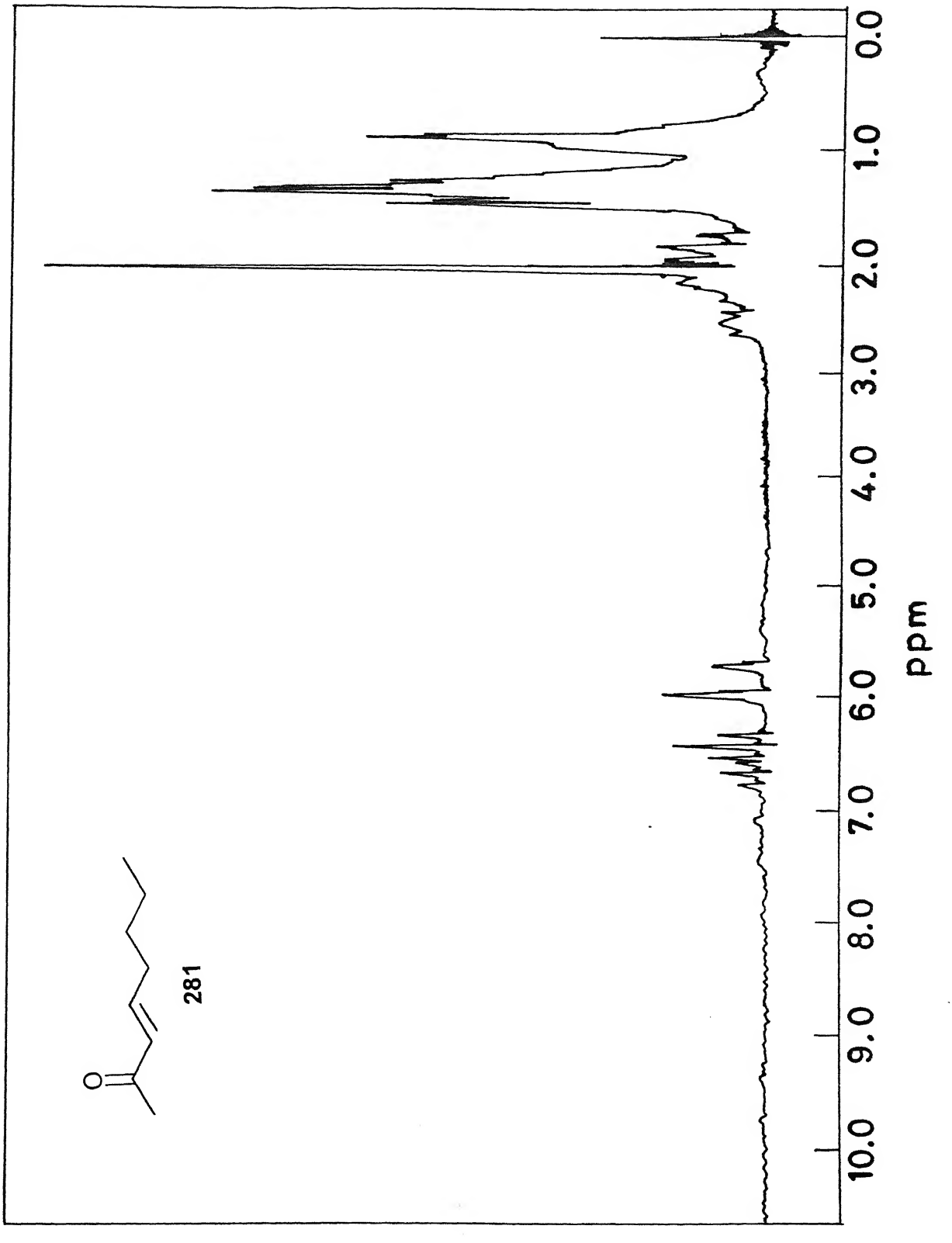
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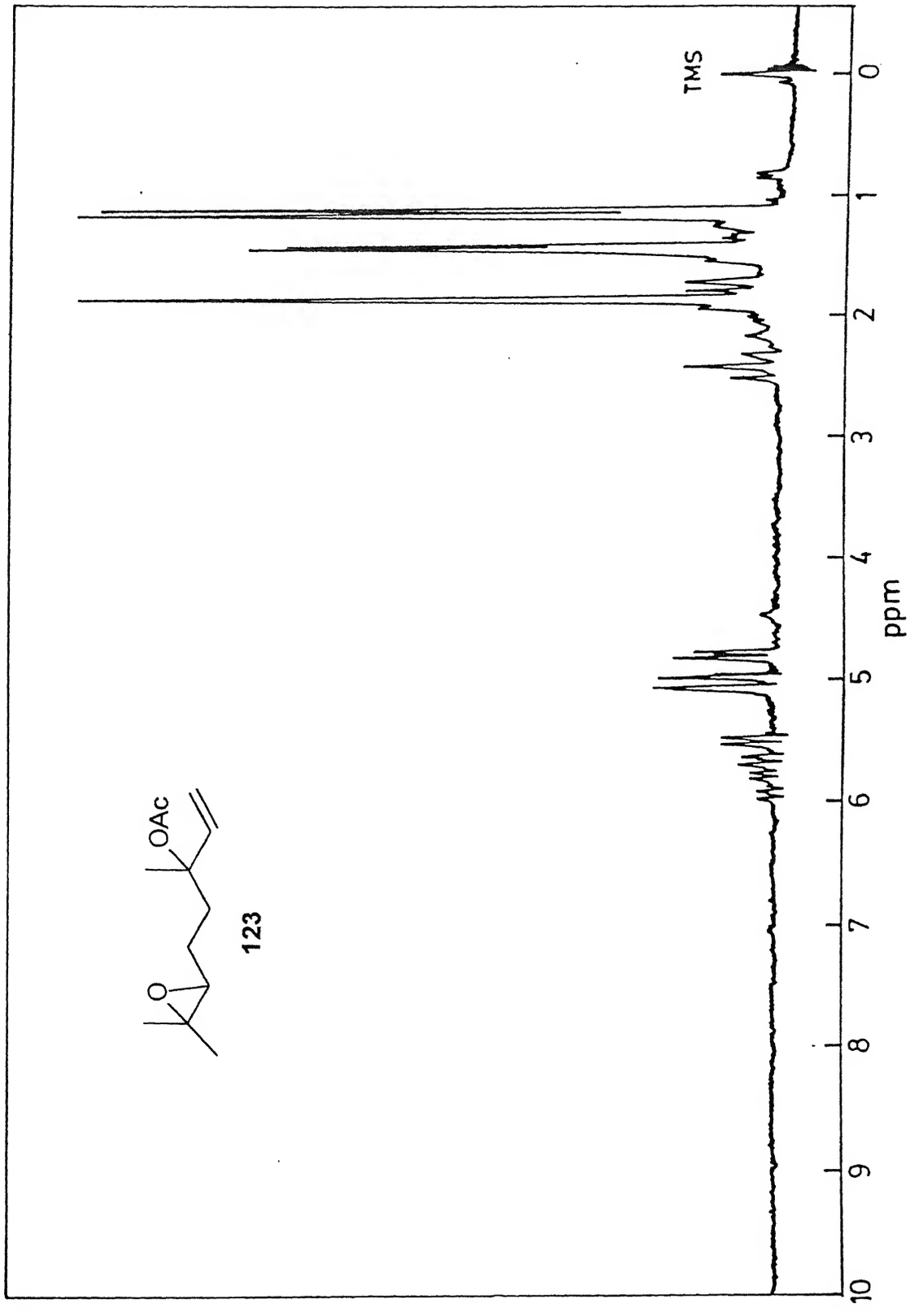
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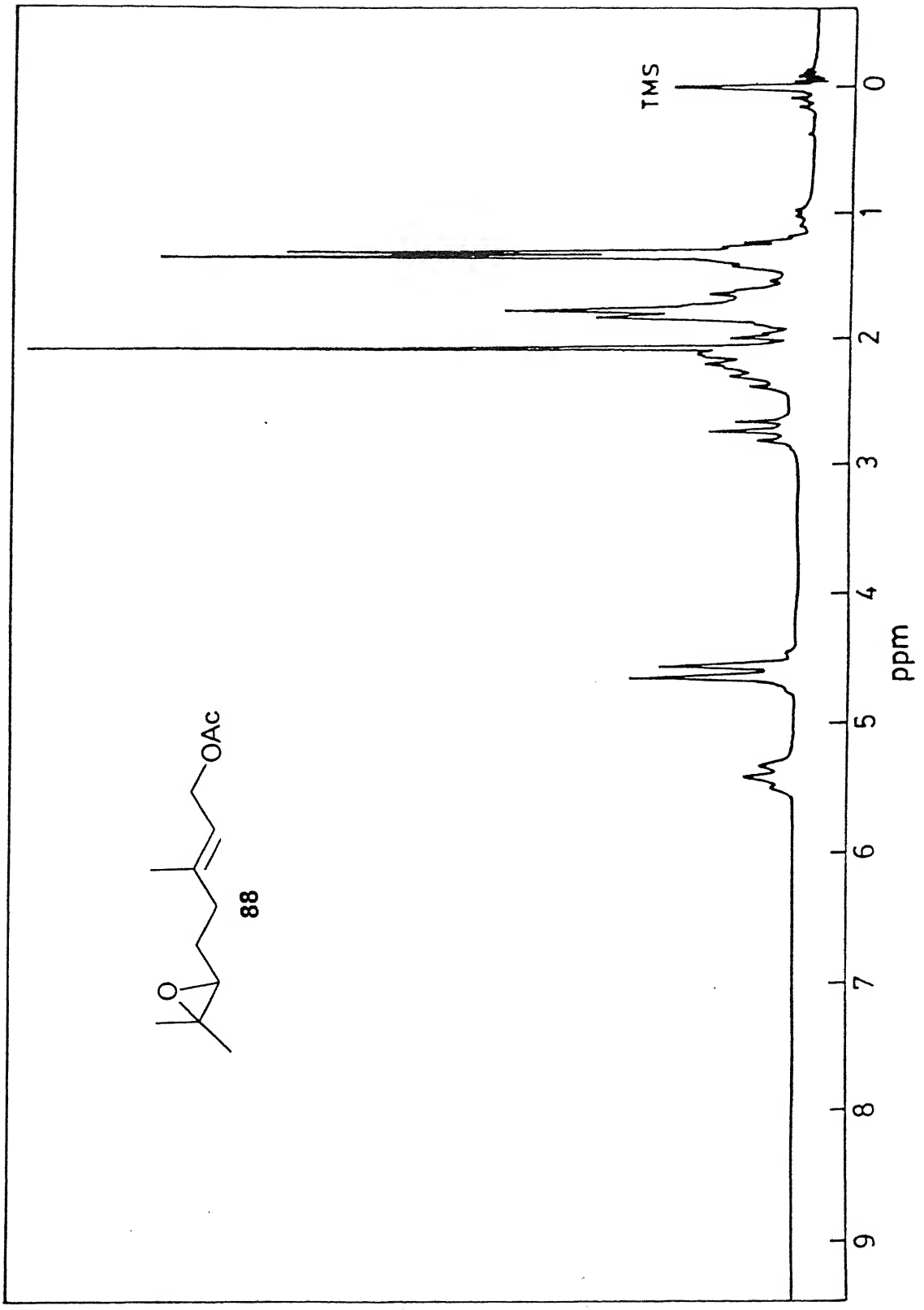
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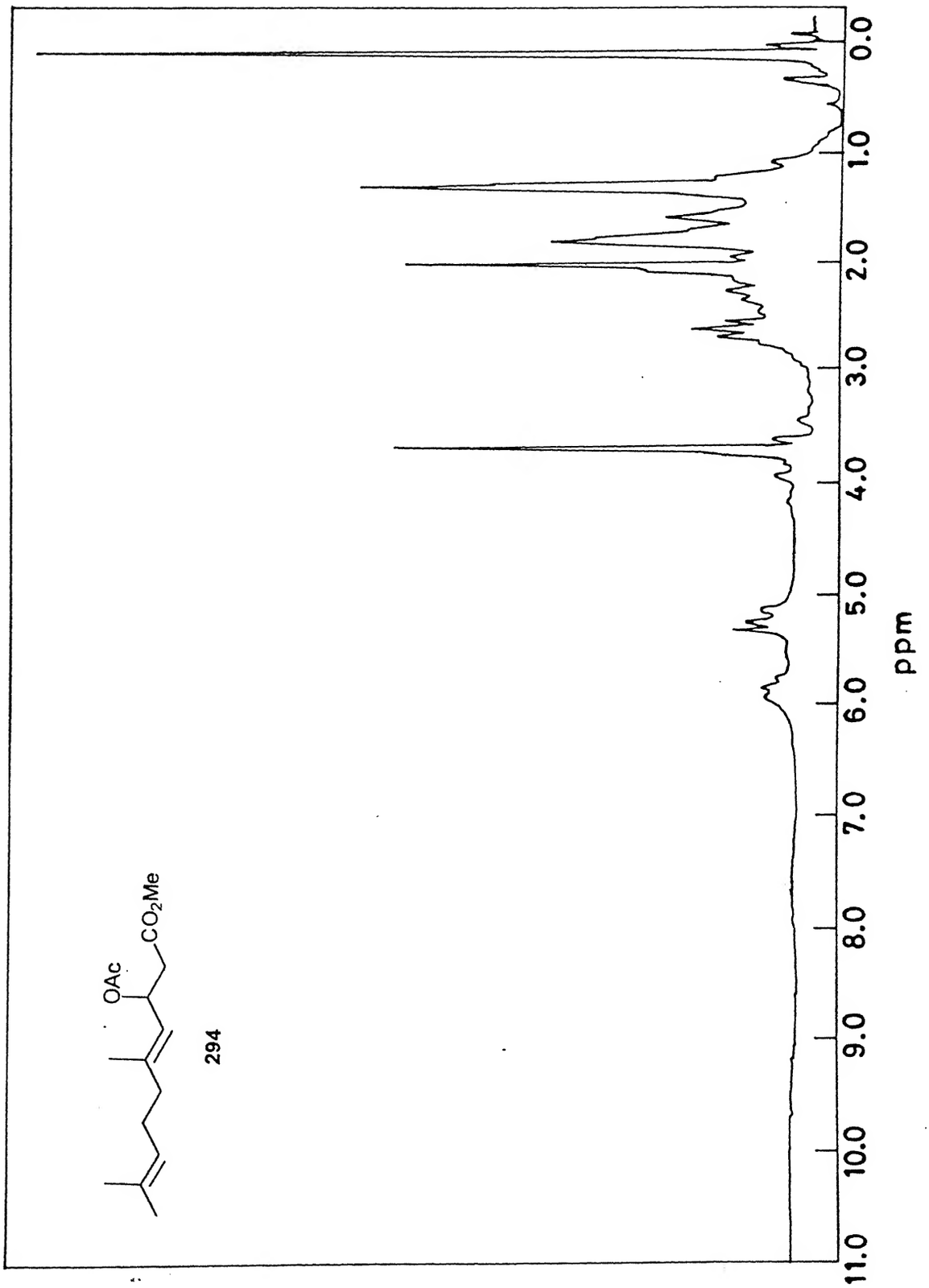
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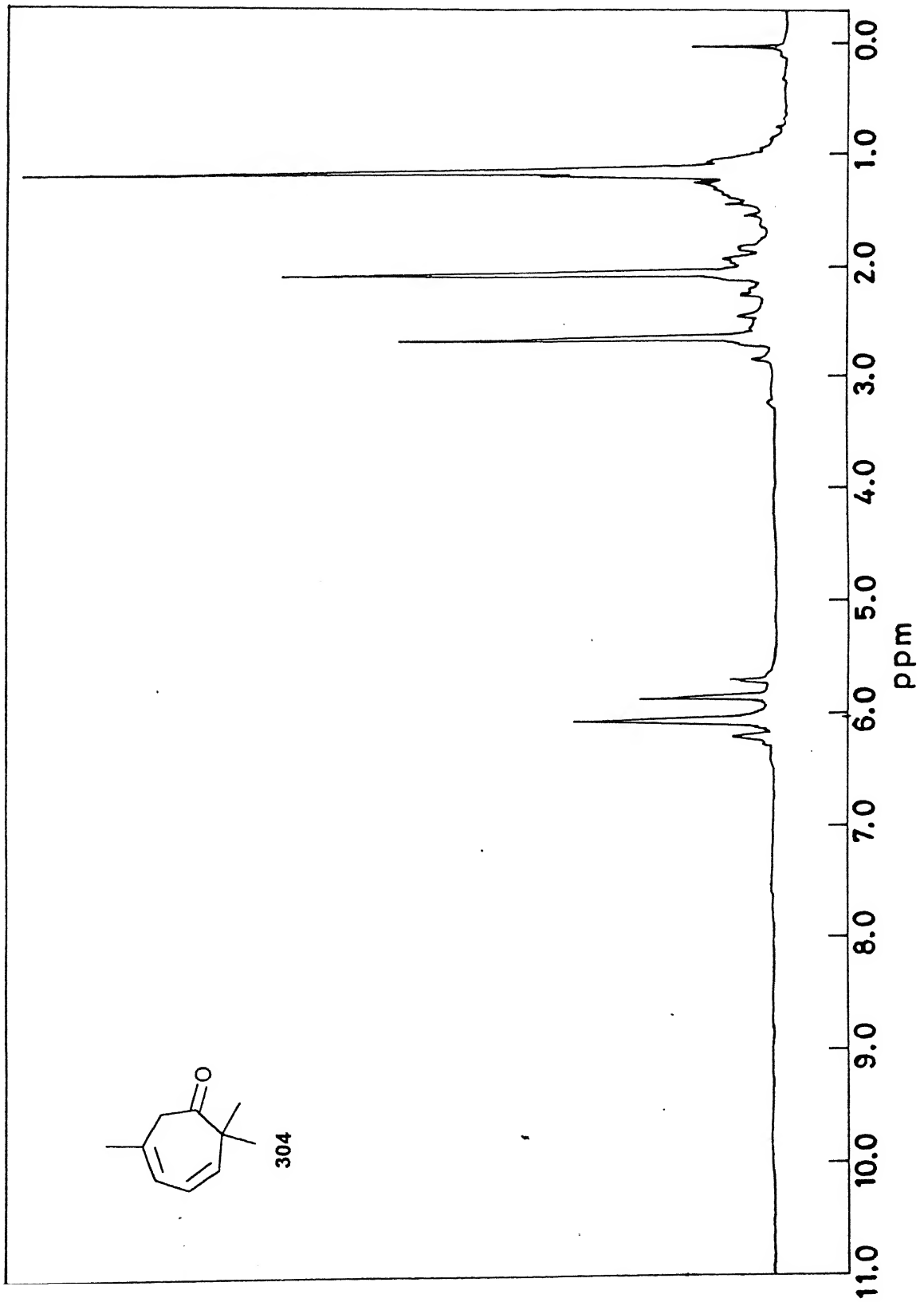
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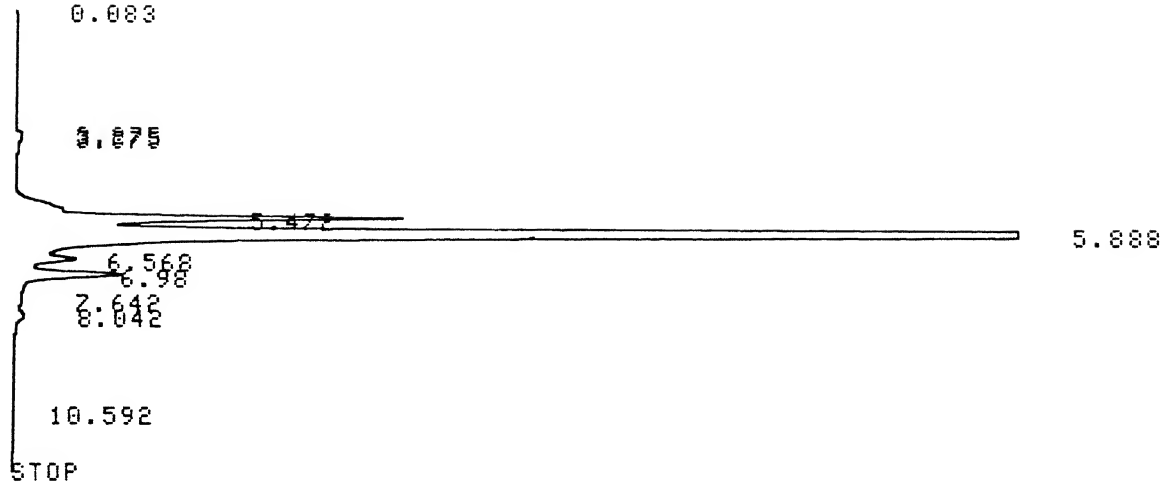

CHROMATOGRAM 1 MEMORIZED

CHROMATOPAC C-R3A FILE 2
SAMPLE NO 0 METHOD 41
REPORT NO 44

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3	3.375	2889	V		0.2242	
4	5.472	157766			12.2462	
5	5.888	1079320	SV		83.7798	
6	6.568	9549	T		0.7412	
7	6.98	32027	T		2.4861	
8	7.642	457	T		0.0354	
9	8.042	3206	T		0.2488	
10	10.592	1081			0.0839	
	TOTAL	1288282			100	

HPLC of Reaction Mixture: Benzyl alcohol **150** , **268** and catalyst **99c.**

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4	5.442	30749	V		0.2814	
5	5.9	10688070	SV		97.8233	
6	7.467	29882	T		0.2735	
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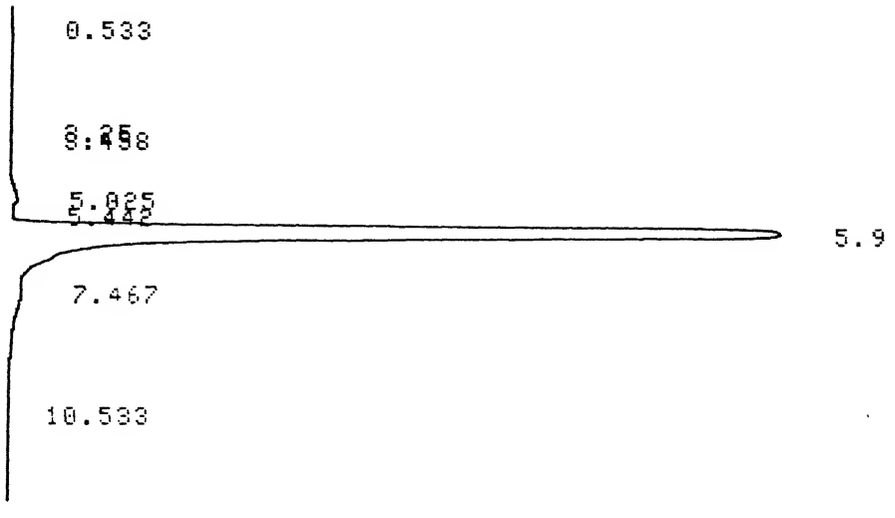
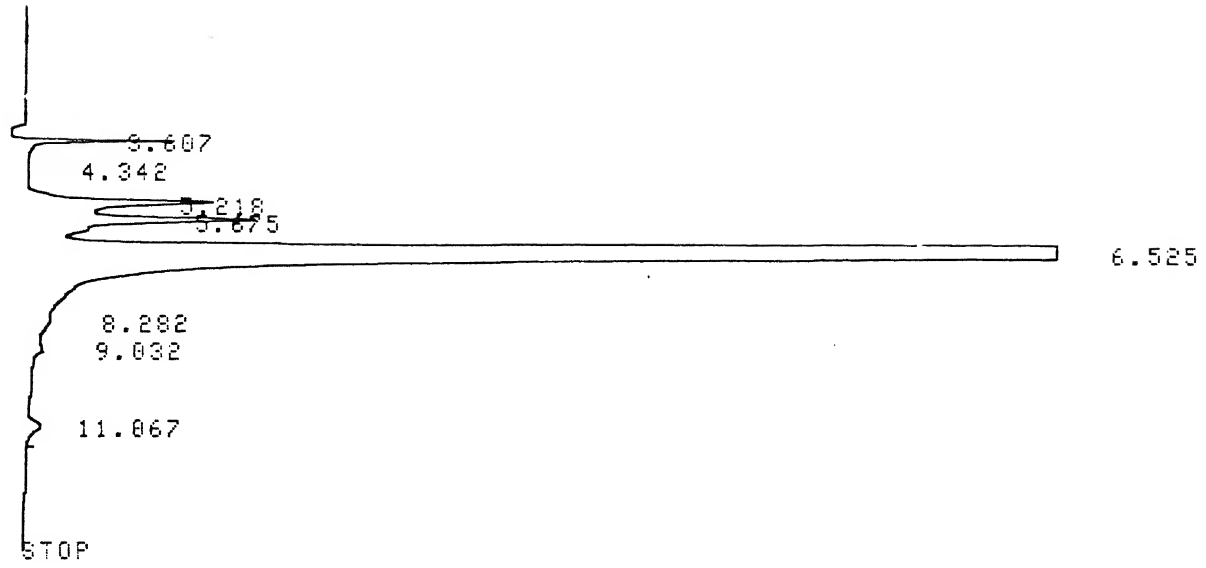


HPLC of Benzaldehyde **159** (Authentic)



C-ROMATOPAC C-R3A
SAMPLE NO 0
REPORT NO 66

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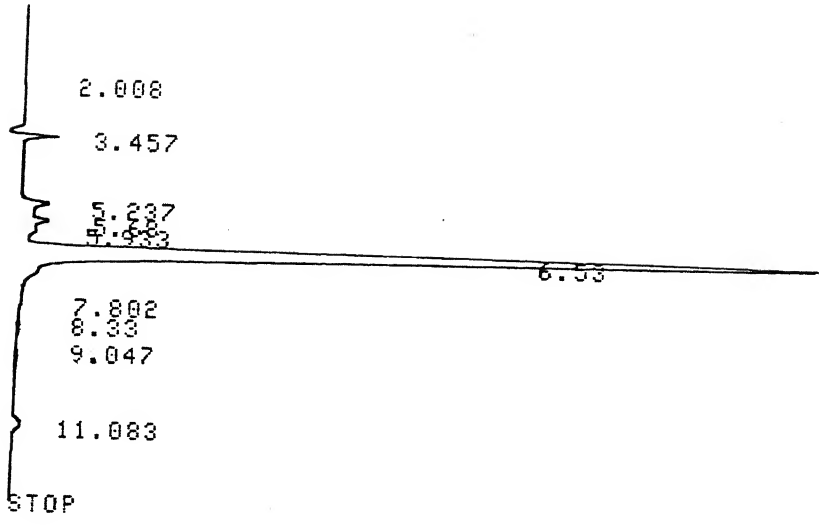
2	4.342	2228	V		0.0561
3	5.218	84685			2.1321
4	5.675	117704	V		2.9634
5	6.525	3719786	SV		93.6525
6	8.282	1258	T		0.0317
7	9.032	3514	T		0.0885
8	11.067	10533			0.2653
	TOTAL	3971900			100

HPLC of Reaction Mixture: Citronellol **320** , **268** and catalyst **99c.**



CHROMATOGRAM 1 MEMORIZED

CHROMATOPAC C-R3A
SAMPLE NO 0
REPORT NO 67

FILE 2
METHOD 41

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	2.008	72			0.016	
2	3.457	15839			3.512	
3	5.237	14340			3.1797	
4	5.68	13316	V		2.9525	
5	5.933	8413	V		1.8653	
6	6.53	391001	SV		86.6966	
7	7.802	407	T		0.0902	
8	8.33	57	T		0.0127	
9	9.047	130	T		0.0287	
10	11.083	7425			1.6463	
	TOTAL	450999			100	

HPLC of Citronellal **321** (Authentic)

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List of Publications

1. Cobalt(II) Catalyzed Reaction of Acetic Anhydride with Aldehydes under Aerobic Conditions : Scope and Mechanism.
   Bhatia, B.; **Punniyamurthy, T.**; Iqbal, J. *J. Org. Chem.* **1993**, 58, 5118.

2. Cobalt(II) Catalysed Reaction of Alkenes with Aliphatic Aldehydes and Molecular Oxygen : Scope and Mechanism.
   Bhatia, S.; **Punniyamurthy, T.**; Bhatia, B.; Iqbal, J. *Tetrahedron*, **1993**, 49, 6101.

3. Cobalt(II) Catalysed Reaction of Enolizable Aldehydes with Alkenes in the presence of Dioxygen : The Role of Acyl Radical.
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4. Cobalt(II) Catalysed Epoxidation of Unfunctionlised Alkenes with in situ Generated Hydroperoxide from 2-Oxocyclopentanecarboxylate and Molecular Oxygen.
   Punniyamurthy, T.; Bhatia, B.; Iqbal, J. *Tetrahedron Lett.* **1993**, 34, 4657.

5. Cobalt(II) Schiff Base Complex Catalysed Oxidation of Alcohols with Dioxygen in the Presence of Ethyl 2-oxocyclopentanecarboxylate.
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7. Cobalt(II) Catalysed Synthesis of 1,2-Diones from Aromatic Aldehydes in the Presence of n-Butanal.
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8. Cobalt(II) Catalysed Oxidation of Alcohols in the Presence of Molecular Oxygen and Isobutanal.
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9. Cobalt-Schiff Base Complex Catalysed Oxidation of Alkenes with Dioxygen in the Presence of β-Ketoester : Allylic Oxidation versus Double Bond Attack.
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10. Cobalt(II) Schiff Base Complex Catalysed Oxidation of Alkenes, Benzylic Substrates and Alcohols with Molecular Oxygen.
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